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Editorial

ARCHIVES OF SURGERY

NEW EDITORIAL DEVELOPMENTS

Development of surgery in the United States has been unprecedented for its rapidity its quality and its scientific character. Few if any would contest the claim that today American surgery leads all the world. In 1920 when the ARCHIVES OF SURGERY was established by the American Medical Association there were but two important periodicals in the surgical field in this country. The space available was hardly sufficient for the publication of all contributions of value—seldom was it possible to publish articles of more than eight or ten pages. These restrictions prevented the publication of many important surgical contributions especially in the field of experimental surgery. It is not surprising therefore that the ARCHIVES OF SURGERY has become in the intervening years the leading publication in the field of experimental surgery and that references to articles published in its pages constitute a large part of the bibliographies of articles on surgical subjects published in foreign periodicals. In every survey of bibliographic references that has been made references to the ARCHIVES indicate that it has been the leading source of consultation in the last two decades.

The highly technical character of much of the material that has appeared in the ARCHIVES OF SURGERY has tended to divert attention to some extent from the ARCHIVES to other surgical publications which have stressed more particularly contributions in the field of clinical surgery and articles dealing with modifications in surgical technic. The unfortunate illness of Dr. Dean Lewis, Editor in Chief of the ARCHIVES OF SURGERY since it was established, brought to the attention of the Board of Trustees of the American Medical Association some of these special problems associated with this publication.

After much consideration it was determined to expand the Editorial Board of the ARCHIVES and to modify the nature of the contents of the periodical in order to make it fulfil more completely its original purpose. Four additional members have now been added to the Editorial Board: Dr. Arthur W. Allen, Boston; Dr. Alfred Blalock, Nashville, Tenn.; Dr. W. E. Dandy, Baltimore; and Dr. L. R. Dragstedt, Chicago. Dr. Waltman Walters has been made chairman pro tem during the incapacity of Dr. Lewis. It has been decided to publish papers dealing with clinical investigation on surgical problems as well as articles which concern developments in the various special fields of general

surgery. Collective reviews will be published from time to time, written by competent investigators who have devoted themselves particularly to special subjects and who will be invited by the editors to develop such reviews. The ARCHIVES will provide prompt publication each month of short preliminary reports of noteworthy surgical advances made by its contributors.

These decisions have been reached after careful consideration of the problems in conferences of the Editorial Board and of members of the Editorial Board with the Board of Trustees. It is anticipated that the surgeons of the United States will welcome the opportunity for more prompt publication in the field of surgery and the availability of the ARCHIVES as an authoritative medium for the recording of surgical advancement.

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LIPID AMINO NITROGEN CONTENT OF THE BLOOD IN DISEASES OF THE LIVER AND OF THE BILIARY TRACT

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AND

ROBERT A MOORE MD

NEW YORK

Despite many experimental and clinical investigations knowledge of the exact nature of the substances and reactions involved in the process of coagulation of the blood is still incomplete. Information concerning the defects of coagulation present in such conditions as hemophilia, jaundice and purpura is even more deficient. Until these fundamental defects are elucidated it is evident that the treatment of these conditions must remain empiric and that the prognosis for any given patient will continue to be uncertain.

Eagle¹ has recently summarized the available evidence on the clotting mechanism and supported the theory that the formation of a blood clot is the result of two basic reactions. The first is the reaction between prothrombin, calcium and a tissue or platelet derivative (thromboplastin) to form thrombin, the second the action of thrombin on fibrinogen to form fibrin. A substance, antithrombin normally present in the circulating blood, or heparin, prepared artificially from dog's liver, may prevent the coagulation of blood by inhibiting the formation of thrombin from its precursors.

The tendency to hemorrhage seen in some cases of obstructive jaundice is particularly serious because many of the patients require surgical procedures to avert the disastrous effects of prolonged cholemia. Hemorrhage plays a major role in the relatively high postoperative mortality of this condition and has prompted many investigations of the clotting mechanism and its defects. Abnormalities or deficiencies in practically all of the recognized factors have been sought for, with varied success.

From the Departments of Surgery and Pathology, the New York Hospital and Cornell University Medical College.

1 Eagle, H. Medicine 16:95, 1937.

In the course of investigations into the hemorrhagic tendency in jaundice, our attention was directed by some experiments performed by Hellman - toward a study of the possible role of alterations of the lipid amino nitrogen of the blood as a factor in this diathesis. Howell³ ascribed the coagulating activity of lipid extracts of the tissues to the monoaminophospholipid cephalin. Recent work of certain investigators⁴ casts doubt on the role of cephalin as the thromboplastic substance. Nevertheless, it is conceivable that thromboplastic activity may be due to some substance closely related to cephalin.

The development by Van Slyke and his associates⁵ of new procedures for the determination of the blood lipids has made possible an approach to the problem of the relation of amino lipids to coagulation of the blood by quantitative chemical methods. The chemical method is not specific for cephalin but determines all the primary amino nitrogen in the soluble extractives of the blood that are soluble in alcohol and ether or in purified petroleum benzene (petroleum ether). In the presence of phospholipids a small amount of urea, a compound with a primary amino group which reacts with nitrous acid, is also dissolved in the extractives.

The first experiments involved determination of the lipid amino nitrogen content of the blood of dogs after experimental ligation of the common bile duct. In the first animal after a control period of forty days, during which time the values for lipid amino nitrogen in 9 determinations ranged between 1.8 and 3 mg per hundred grams of whole blood, the common duct was doubly ligated and divided. This procedure produced a transient rise, followed by a fall to 0.6 mg after thirty days (chart 1).

Further experiments showed that a progressive fall in the lipid amino nitrogen content of the blood after ligation of the common bile duct was not a constant finding. In some dogs there was a conspicuous increase of the lipid amino nitrogen before death (chart 2). At autopsy the pathologic conditions observed in dogs with a progressive decrease were different from those in dogs with a terminal increase. In the former, obstructive biliary cirrhosis was the only change in the liver, while in the latter there were cholangitis and multiple abscesses of the liver. In 1 animal in which the lipid amino nitrogen decreased, death resulted from hemorrhage into the operative field after a cholecysto-

2 Hellman, L. M., Moore, R. A., and Andrus, W. DeW. *Proc. Soc. Exper. Biol. & Med.* **36** 176, 1937.

3 Howell, W. H. *Am. J. Physiol.* **29** 187, 1911.

4 Fischer, A., and Hecht, E. *Biochem. Ztschr.* **269** 115, 1934. Charles, A. F., Fisher, A. M., and Scott, D. A. *Tr. Roy. Soc. Canada (Sect. 5)* **28** 49, 1934.

5 Kirk, E., Page, I. H., and Van Slyke, D. D. *J. Biol. Chem.* **106** 203, 1934.

duodenostomy. In the other animals there was no apparent correlation between the altered values for lipid amino nitrogen and a tendency to hemorrhage in dogs with obstructive jaundice.

Although the results in animals were inconclusive it seemed desirable to study the lipid amino nitrogen in man. Determinations on 22 patients without clinically detectable disease of the liver gave an average value

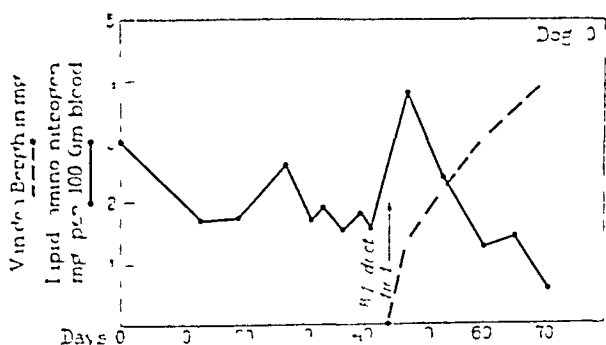


Chart 1—Lipid amino nitrogen content of the blood after experimental ligation of the bile duct

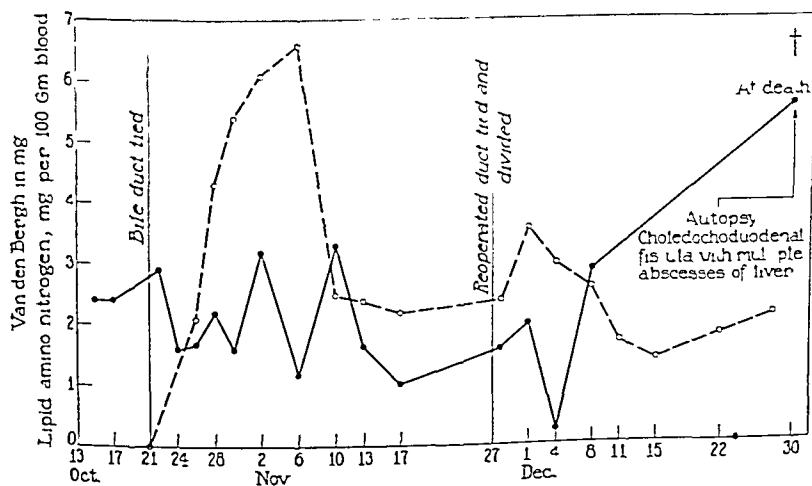


Chart 2—Increase of the lipid amino nitrogen content of the blood before death

of 1.24 per hundred grams of blood, with a standard deviation of 0.62. As is shown in the table, 128 determinations on 43 patients with jaundice or with other conditions associated with hemorrhage or damage to the liver were made.

One of the first patients studied had severe obstructive jaundice associated with carcinoma of the cystic duct. Death occurred nine days

after an exploratory laparotomy, with hemorrhage into the wound and in the tissues about the carcinoma. In this patient (chart 3) the value for lipid amino nitrogen was elevated above the average normal and terminally reached the extraordinarily high level of 12 mg per hundred grams of blood. Two additional patients with hemorrhage and terminal increase of the lipid amino nitrogen to 4 and 6 mg respectively have been observed. The occurrence of extensive hemorrhage in these 3 patients at a time when the lipid amino nitrogen was increased throws doubt on the role of lipid amino compounds in the coagulation of blood. There are two possible explanations of the discrepancy: first, that nonlipid amino compounds, such as urea, were

Conditions in Which the Lipid Amino Nitrogen Content of the Blood Was Studied

Diagnosis	No of Cases	No of Determinations
Common duct stone	4	30
Catarrhal jaundice	5	14
Carcinoma of the bile ducts or pancreas	5	38
Other carcinomas	3	3
Hemolytic jaundice	2	5
Hepatic disease *	3	6
Thrombopenic purpura †	2	8
Chronic cholecystitis	3	3
Hemorrhage ‡	6	7
Perniciou anemia	1	1
Goiter	3	3
Miscellaneous conditions (patients moribund) ‡	4	4
Diabetes	1	2
Chronic cholangitis	1	4
	43	128
Controls	22	23
	65	151

* One case each of abscess of the liver, arsphenamine poisoning and atrophy of the liver

† Due to causes other than jaundice or thrombopenic purpura

‡ One case each of abscess of the brain, septicemia, abscess of the lung and fracture of the skull

included in the extractives of the blood, and second, that the lipid extractives have an optimal concentration, above or below which they are ineffectual as thromboplastic substances.⁶

Five patients (chart 4) with catarrhal jaundice showed no elevation of the lipid amino nitrogen above normal despite icteric indexes which at times reached 150. The same findings were observed in 4 patients with stone in the common bile duct. In these 9 instances of jaundice uncomplicated by severe damage to the liver the values for lipid amino nitrogen remained normal.

Two additional patients with carcinomatous obstruction of the biliary tract are of importance in bridging the gap between the findings

⁶ Wadsworth, A., Maltaner, F., and Maltaner, E. J. Immunol. 30: 417,

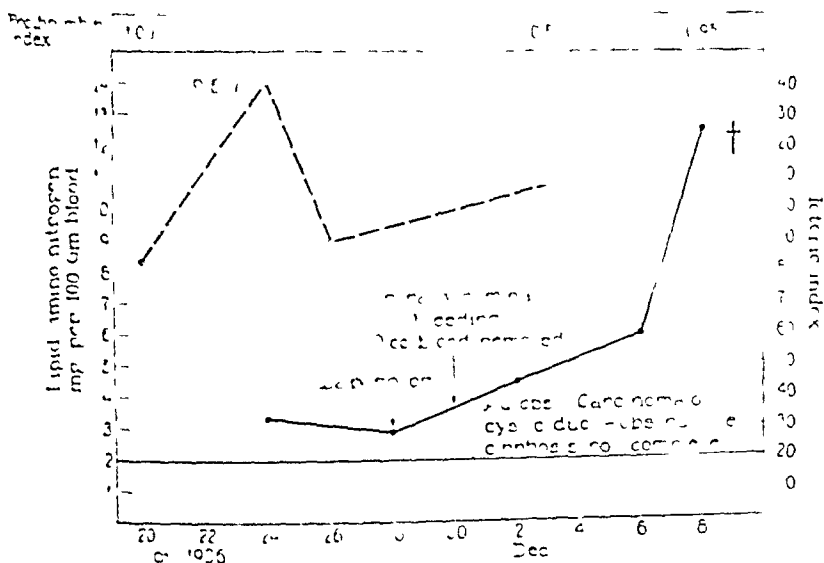


Chart 3—Antemortem elevation of the lipid amino nitrogen content of the blood at a patient with carcinoma of the cystic duct and obstructive cirrhosis

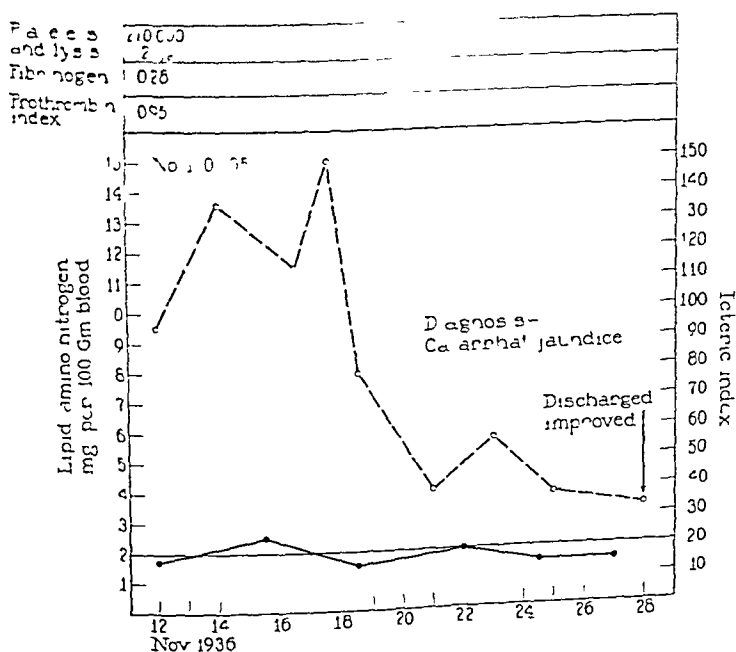


Chart 4—Lipid amino nitrogen content of the blood in a case of catarrhal jaundice

in patients with hemorrhage and increased values of the lipid amino nitrogen content of the blood and those with no hemorrhage and with normal values. In 1, a patient with obstructive jaundice (icteric index, 80) due to carcinoma of the head of the pancreas, who was not operated on but died of bronchopneumonia, the values for lipid amino nitrogen remained within normal limits. In the other, a patient with carcinoma of the gallbladder, metastases to the liver and obstructive cirrhosis (determined by biopsy), the value reached 6 mg before death. Neither patient showed evidence of hemorrhage.

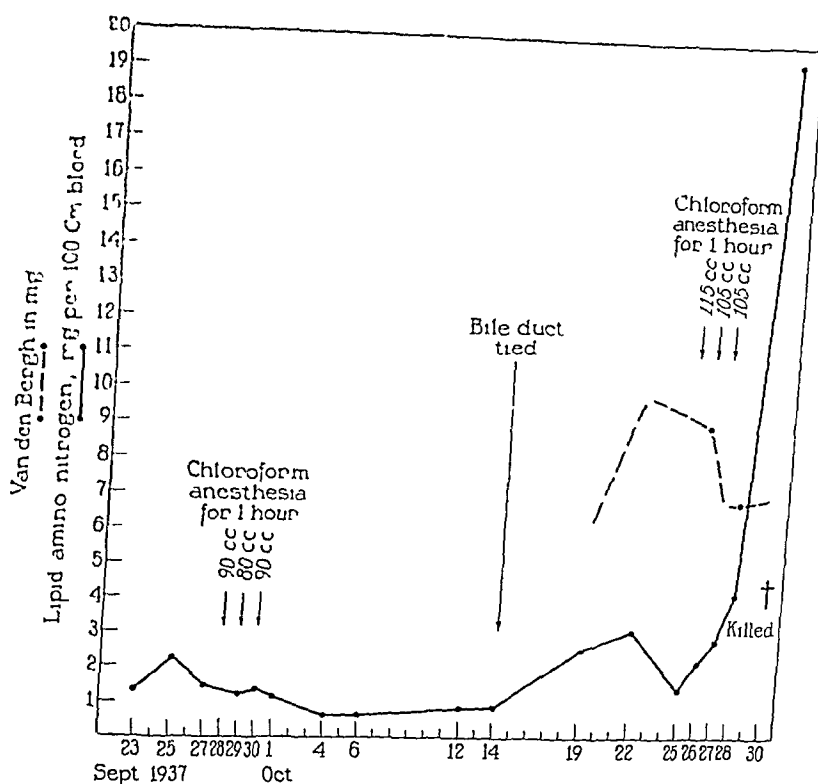


Chart 5—Effect of chloroform anesthesia, with and without obstructive jaundice, on the lipid amino nitrogen content of the blood

Three patients with carcinoma of organs other than the liver, pancreas or biliary ducts uniformly showed values for lipid amino nitrogen within normal limits. The same was true of 4 patients moribund from causes not related to disease of the liver.

It would seem, therefore, that the findings in man have a similarity to those in dogs. When severe damage to the liver was present, the values for lipid amino nitrogen were elevated above 2 mg and tended to ascend still higher before death, while patients with jaundice, however severe, unassociated with demonstrable damage to the liver showed values below 2 mg at all times.

In 2 patients with congenital hemolytic jaundice and in 2 patients with thrombopenic purpura the values for lipid amino nitrogen were normal and showed no change after splenectomy.

With this information obtained from observations in man, indicating the significance of damage to the liver as a factor in the elevation of the lipid amino nitrogen content of the blood, further experiments were carried out on animals with substances known to produce damage to the liver. These included prolonged chloroform anesthesia and the injection of phosphorated oil and of carbon tetrachloride. In animals without obstruction of the common duct no significant changes in the levels of lipid amino nitrogen resulted. On the contrary, the administration of chloroform to 3 animals with obstruction of the common bile duct was followed by a conspicuous increase of the lipid amino nitrogen in the blood (chart 5). In 1 animal with obstruction of the common bile duct the injection of phosphorated oil did not result in an increase. These observations indicate that the liver of an animal with obstructive jaundice is more sensitive to damage than that of a normal animal. The livers of the animals with obstructive jaundice and chloroform poisoning showed profound fatty degeneration and necrosis of the entire lobule together with the usual changes of obstructive cirrhosis.

In a further attempt to shed some light on the metabolism of lipid amino nitrogen experiments on the effect of hemorrhage and of a permanent biliary fistula were carried out. In 2 dogs, the withdrawal of sufficient blood to produce a reduction in blood volume of approximately one third in a three day period failed to cause any appreciable alteration in the level of the lipid amino nitrogen of the blood. In man, 7 determinations in 6 patients with severe hemorrhage from peptic ulcer were within the normal range. In a dog with a biliary fistula there was no significant change in the lipid amino nitrogen in a period of sixty days.

CONCLUSIONS

- 1 The normal lipid amino nitrogen content of the blood averages 1.24 mg per hundred grams of whole blood, with a standard deviation of 0.62.

- 2 In patients with obstructive or hemolytic jaundice but without evident damage to the liver the lipid amino nitrogen content of the blood is within normal limits.

- 3 In patients with obstructive jaundice and damage to the liver there is consistent elevation of the lipid amino nitrogen content of the blood above 2 mg per hundred grams of whole blood.

- 4 There is no apparent correlation between the hemorrhagic diathesis in obstructive jaundice and the level of lipid amino nitrogen in the blood.

LARYNGEAL SPASM AND SO-CALLED TRACHEAL COLLAPSE

EXPERIMENTAL AND CLINICAL STUDIES

WARREN H COLE, MD

CHICAGO

The experiments herein reported were performed in an attempt to explain serious stridor arising in a patient on whom thyroidectomy was being performed

The patient was a middle-aged man with an average degree of hyperthyroidism of a toxic diffuse type. A routine thyroid incision, splitting the ribbon muscles in the midline, was made with the patient under ethylene anesthesia. When hemostats were put on the capsule of the right lobe preparatory to excision of the lobe, mild stridor developed. During the process of excising the lobe, mild tension was applied on it to effect delivery. The stridor increased markedly, until it became so severe as to indicate almost complete obstruction of the airway by the time the excision had approached the trachea. A rapid search was made for the recurrent laryngeal nerve, it was found lying in the usual position, but no clamps were within $\frac{1}{4}$ inch (0.6 cm) of it at any point. Since there appeared to be no hemostats on the nerve, but more particularly since the stridor had developed before the thyroid lobe was cut, it was felt the stridor was of reflex origin and not the result of direct trauma to the nerve. The operation was stopped and all tension released for at least a minute, but the stridor persisted. The isthmus was then rapidly undercut and the trachea exposed. The trachea was no larger than a lead pencil and appeared bloodless. Again all tension was released, the weight of the clamps being taken off the neck, and two or three minutes elapsed before it was decided that a tracheotomy should be done. By this time the patient was extremely cyanotic and was getting practically no air through the larynx. However, at this point the airway began to open, and after about four or five minutes the patient was breathing in a normal fashion. The anesthetist had been giving ethylene but had changed to pure oxygen during the respiratory difficulty. It appears that the patient's relief was caused more by the release of the trachea from the isthmus, with consequent relaxation, and by stopping the operative procedure than by changes in the anesthetic procedure alone. When the trachea was observed again after the patient had recovered from the laryngeal obstruction, it had enlarged to at least the size of one's index finger and was unusually pink. This marked change in size was noted by the entire operating team and was too pronounced to be an erroneous observation. It appeared then that the trachea had actually undergone a spasm, which had produced a marked decrease in size, or that negative pressure incident to a laryngeal obstruction was instrumental in

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From the Department of Surgery, University of Illinois, College of Medicine, the Illinois Research Hospital and the State Department of Public Welfare

causing a partial collapse of the tracheal walls. However, while the necessity of tracheotomy was being debated the patency of the lumen was proved by aspirating the trachea with a hypodermic needle and syringe to identify it in case tracheotomy would have to be done. The trachea was so small and covered with sufficient areolar and fibrous tissue that one could scarcely be certain of its identity. The patient recovered so well from the respiratory obstruction that the operation was continued and the left lobe re-ected. This was done without any evidence of respiratory obstruction. At no time in the postoperative course did the patient have any respiratory difficulties. Laryngoscopic examination of the vocal cords revealed normal action.

Numerous instances of a similar but less severe nature have been encountered by me as well as by practically all other surgeons. In my experience stridor develops most commonly while the superior thyroid artery is being isolated and ligated. I have heard of several tracheotomies being performed under similar circumstances but with immediate recovery after operation thus allowing the tracheotomy tube to be removed within twenty-four hours. The routine anesthetic in use during my own work has been ethylene. Occasionally ether has been given in experimental fashion during the mild episodes of stridor. The ether actually appeared to be of definite though mild assistance in eliminating stridor. Obviously the anesthetists make all attempts to eliminate anoxia during the complication. Anoxia will undoubtedly be associated with all instances of severe adductor spasm of the larynx. However, it is probable that the anoxia per se does not increase the spasm but in reality tends to relieve the condition by its reflex action toward dilation of the larynx. Anesthetists have noted at times that administration of oxygen relieves stridor. In some instances it is probable that relief is brought about not by the oxygen per se but by dilution of the anesthetic agent, which by reflex action was the primary cause of the laryngeal (or tracheal) spasm. In reviewing the cases it does not appear that the patients suffering this complication had preliminary anoxia incident to the anesthetic. Several theories may be proposed to explain stridor, namely, laryngeal spasm, tracheal spasm and tracheal collapse. It was because of the inability to explain this complication that the experiments herein described were conducted. When stridor occurs during manipulation of the superior pole, injury to the superior laryngeal nerve must be considered, as is discussed later. Without doubt light anesthesia encourages development of stridor.

ANATOMY AND PHYSIOLOGY

Trachea—The cartilaginous rings of the trachea varying between fifteen and twenty in number, are horseshoe shaped and connected to each other by the fibroelastic membrane in which the rings are embedded. The posterior fourth of the trachea is made up of the trachealis muscle which in the human being is attached primarily to

the tips of the rings, but some fibers may be attached to the inner and outer surfaces of these rings near the tips as well as to the fibroelastic membrane between the rings. In the dogs examined by me a portion of the muscle was attached to the tips of the rings, but most of it was attached to the outer surface of the rings and the adjacent fibroelastic membrane. Contraction of the trachealis muscle will appreciably narrow the width of the tracheal lumen. The amount of constriction attainable by contraction of the trachealis muscle varies considerably, even in normal persons because of the variation in the strength of the carti-

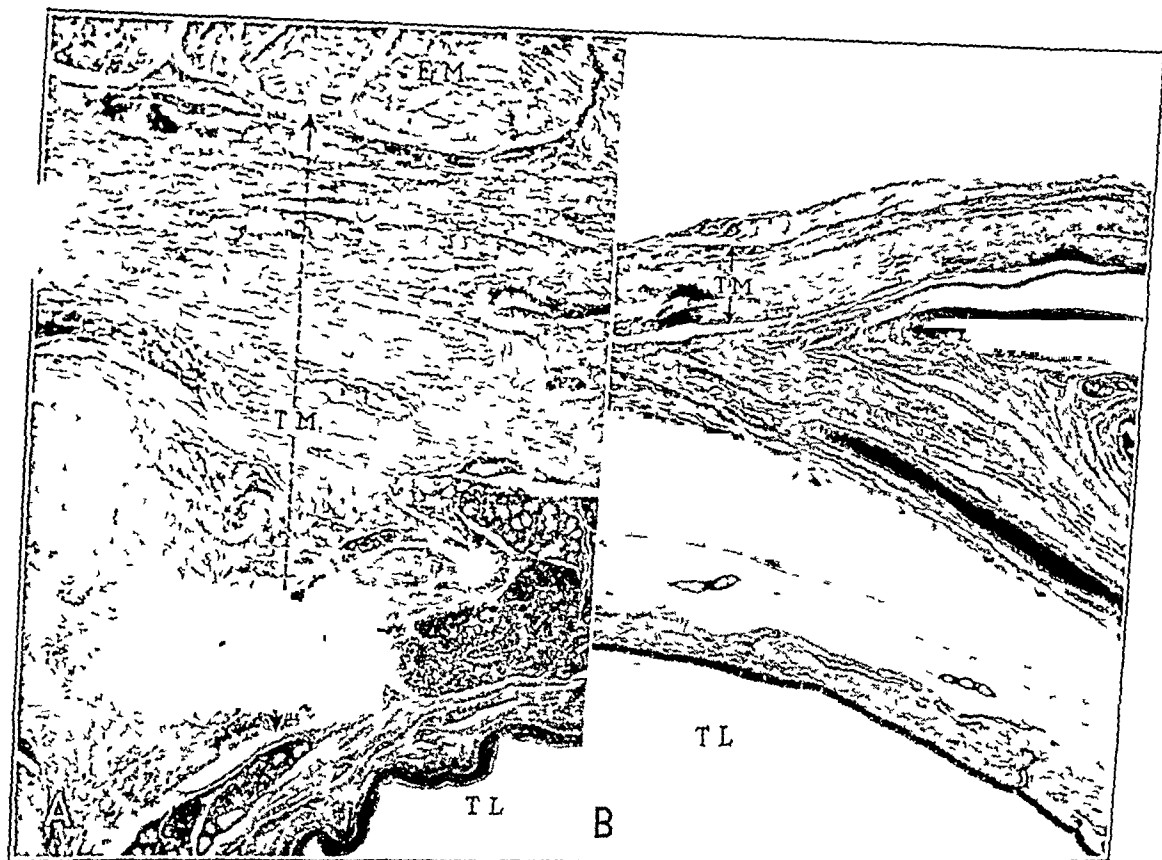


Fig 1—*A*, low power photomicrograph showing a section through the posterior portion of the trachea of a human being. *TM* indicates the tracheal muscle, *TL*, the tracheal lumen, and *EM*, the esophageal muscles. *B* low power photomicrograph of the posterior portion of the dog's trachea. Note that the thickness of the trachealis muscle which is indicated in each photomicrograph (*TM*) is comparatively much greater in the human being than in the dog. Theoretically the trachealis muscle of the human being would be capable of more contraction than that of the dog, but proof of this is not at hand.

laginous rings. A decrease in the strength or support offered by these rings is noted in certain constitutional diseases, but more particularly when a thyroid nodule compresses the trachea over a long period. In the latter instance, as will be discussed later, the erosion or atrophy

of a few cartilaginous rings at the site of pressure by the adenoma may be almost complete. Experiments to be described show conclusively that stimulation of the trachealis muscle of the dog with an electric current produced a pronounced contraction. To my knowledge the results of similar experiments on the human trachea are not available but a comparison of the amount of trachealis muscle shows a greater quantity in the human being than in the dog (fig 1) implying that the constricting effect on the trachea could be equally if not more prominent in the human being than in the dog. The trachealis muscle in the human being is supplied by the recurrent laryngeal nerve and in the dog by the pararecurrent nerve (fig 2). Although fixed posteriorly to prevent traction on

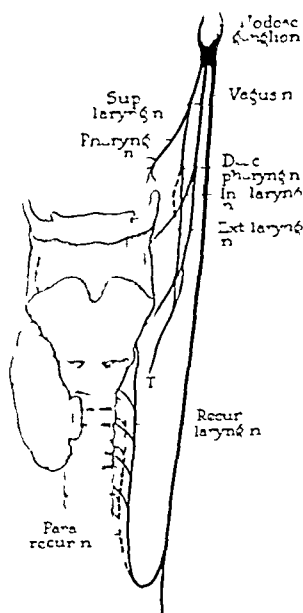


Fig 2—Nerve supply of the larynx. The nerves shown by the dotted lines are the pararecurrent nerve and a descending branch of the pharyngeal nerve which represent the two main points of difference in the nerve supply of the larynx in the dog and the human being. In the dog the cricothyroid muscles are frequently innervated by a branch of the pharyngeal ramus of the vagus nerve.

the lungs by movement of the head the trachea is elastic and thereby allows for stretching. Another important protective mechanism afforded by elasticity of the trachea lies in the fact that compression of the trachea by tumors in the neck is minimized by deviation made possible by tracheal elasticity.

The function of the trachealis muscle in primitive life was no doubt primarily related to constriction of the tracheal lumen during expiration, to eliminate as much dead space air as possible thereby aiding in

endurance of the animal as far as activity is concerned. Negus¹ has called attention to the fact that the trachealis muscle is extremely thick in the horse and being attached high on the cartilaginous rings, would by contraction be effective in expelling dead space air during expiration. However, this expiratory movement is not present in the human being, as determined by observation during thyroidectomy. It would appear then that as man developed past the scale where physical endurance was important in the maintenance of life, this function was being lost, although there is good evidence that the trachealis muscle is capable of contraction with consequent narrowing of the lumen of the trachea.

Larynx — Authorities differ as to the number of intrinsic muscles in the larynx, because of the complicated way in which the various muscle bundles intermingle. The numbers given vary between eleven and nineteen. All except the interarytenoid muscles are paired. The intrinsic muscles may be classified into three groups. The constrictor group, including the adductors of the vocal cords, consist of the lateral cricothyroid, the interarytenoid, the thyroarytenoid, the oblique arytenoid and the aryepiglottic muscles. The dilator muscles of the larynx, including the abductors of the vocal cords, are the posterior cricoarytenoid and possibly the thyroepiglottic muscles. A third group is instrumental primarily in modifying tension of the vocal cords. The cricothyroid muscles produce tension on the cords, whereas the internal thyroarytenoid (vocalis) muscles produce relaxation of the cords. In number, mass and muscle power the adductors predominate over the abductors, a factor which in itself may be of importance in explaining the readiness with which adductor spasm is produced.

There is slight difference of opinion regarding the innervation of these muscles. Most textbooks on anatomy state that the cricothyroid muscles are innervated by the external branch of the superior laryngeal nerve and all the remaining intrinsic muscles by the recurrent laryngeal nerve.

There is likewise a difference of opinion regarding the position of the recurrent laryngeal nerve as related to the inferior thyroid artery. Berlin and Lahey² noted that in 18 of 23 cadavers the nerve on the right was anterior to the artery, whereas it was posterior to the artery on the left side in 19 of 22 instances. In 4 of the 19 instances the nerve was posterior to the lower branch but anterior to the upper branch of the

1 Negus, V. E. *The Mechanism of the Larynx*, St. Louis, C. V. Mosby Company, 1930.

2 Berlin, D., and Lahey, F. H. *Dissection of Recurrent and Superior Laryngeal Nerves. Relation of Recurrent to Inferior Thyroid Artery and Relation of Superior to Abductor Paralysis*, Surg., Gynec. & Obst. 49:102, 1929.

artery Nordland³ has stressed the fact that the superior laryngeal nerve is only slightly above the superior thyroid artery and may thus be injured readily during ligation of the superior pole and in certain instances may give rise to changes in the vocal cords Nordland however was unable to confirm the difference in positions of the two nerves which was noted by Berlin and Lahey

Severance of the recurrent laryngeal nerve will obviously lead to paralysis of the intrinsic muscles (except the cricothyroid and possibly the interarytenoid muscle) thereby allowing the cricothyroid tensor adductor to pull the cord to the midline with consequent obstruction to respiration, particularly if both nerves are injured Judd and his associates⁴ performed a series of experiments on dogs and noted that section and ligation of the nerve with linen would lead to permanent paralysis whereas pinching the nerve firmly with a hemostat was followed by temporary paralysis lasting for thirty to sixty days In general experience teaches that practically the same results are to be expected in the human being It should be emphasized here that paralysis of one cord, particularly if not complete may produce no symptoms whatsoever even in the voice, and may not be detected unless laryngologic examination is done Detailed studies have been made by Lemere⁵ on dogs showing the effect of severance of the various nerves on the glottic picture Section of both nerves in the dogs practically always is accompanied by loss of the voice and usually but not always by loss of the voice in the human being

It has been known for a great many years that anesthesia (particularly ether) produces a confusing effect on the results of stimulation of the recurrent laryngeal nerve In 1887 Hooper⁶ noted that stimulation of the recurrent nerve in dogs produced adduction of the cords under light ether anesthesia and abduction under deep ether anesthesia Lemere⁷ noted that in dogs less than 2 months old abduction is always obtained in spite of deep anesthesia regardless of its depth Russel⁸ showed that the fibers of the recurrent nerve were divided

3 Nordland M The Larynx as Related to Surgery of the Thyroid Based on an Anatomical Study, Surg, Gynec & Obst **51** 449 1931

4 Judd E S, New, G B, and Mann F C The Effect of Trauma on the Laryngeal Nerves An Experimental Study Ann Surg **67** 257 1918

5 Lemere, F Innervation of the Larynx Experimental Paralysis of the Laryngeal Nerve, Arch Otolaryng **18** 413 (Oct) 1933

6 Hooper, F H The Recurrent Laryngeal Nerves New York M J **46** 29 1887

7 Lemere, F Innervation of the Larynx IV An Analysis of Semon's Law Ann Otol, Rhin & Laryng **43** 525, 1934

8 Russel, J S R The Abductor and Adductor Fibers of the Recurrent Laryngeal Nerve, Proc Roy Soc London **51** 102 1892

into two groups one of which supplied the abductor muscles whereas the other supplied the adductor muscles. This anatomic separation will no doubt explain some of the inconsistencies known to exist regarding the effect of stimulation of nerves on the laryngeal muscles. It has been suggested that the greater concentration of lipid granules in the abductor than in the adductor muscles may explain the early action of ether on the abductors, but it is doubtful if this is true since in clinical experience serious paralytic effects have been encountered under other anesthetics, such as ethylene and nitrous monoxide.

In 1881 Semon⁹ proposed a rule or law that in partial or incomplete destruction of the recurrent laryngeal nerve the muscles of abduction are affected first. It has been accepted by many, but not those working on the neuromuscular mechanism of the larynx. It may possibly be supported by the experiments of Semon and Horsley,¹⁰ who showed that when the larynx is excised from an animal the abductor muscles are the first to lose their excitability to electric stimulation.

REVIEW OF EXPERIMENTS

The object of these experiments was to determine how much contraction of the trachealis muscle and intrinsic muscles of the larynx could be obtained by electric stimulation and by reflex action such as might be produced by operative trauma about the neck, particularly on the thyroid. Observations on the trachea were made by making a midline incision in the neck, with the dog under ether anesthesia and exposing the trachea. The recurrent and pararecurrent nerves were carefully dissected away from each side so that an incision could be made near the sternum, a tracheal cannula inserted into the distal stump and a rubber tube with a small balloon attached to the end placed in the proximal stump. The rubber tube was connected with a tambour. Although readings could be obtained by using a rubber tambour, the excursions of the lever were much wider if a cylinder type of tambour was used. Observations on the action of the vocal cords were obtained in a similar way, the balloon being inserted into the larynx from the mouth as well as from the trachea. The stimulus used was a faradic current derived from an ordinary dry cell battery inducting coil, only a small portion of the current obtainable from the two batteries being used.

When the trachealis muscle was stimulated directly with the balloon in place, there was a pronounced slow contraction of the smooth muscle

⁹ Semon, F. Proclivity to Disease of Abductor Fibers, *Arch. Laryng.* **2** 197, 1881.

¹⁰ Semon, F., and Horsley, F. On an Apparently Peripheral and Differential Administration of Ether on the Laryngeal Nerves, *Brit. M. J.* **2** 405, 1886.

type (fig 3) The muscle apparently fatigues slowly The frequent oscillations of the tracing lever represent respiratory movements and can be eliminated to a great extent with no appreciable loss in accuracy of the response, by applying a variable amount of tension on the dog's tongue or larynx The contraction can be seen readily with the naked eye (fig 4) As the muscle contracts it attains the shape of a roll of muscle fibers frequently approximating the ends of the cartilaginous rings The diameter of the trachea lessens about 2.5 mm most of this decrease in the lumen takes place in the lateral diameter but there is occasionally slight shortening in the anteroposterior direction depending somewhat on the shape of the trachea and on similar factors As would be expected the maximum contraction was noted in young dogs In old dogs palpation of the trachea would readily show a lack of elasticity of the rings as compared to the elasticity noted in young animals For

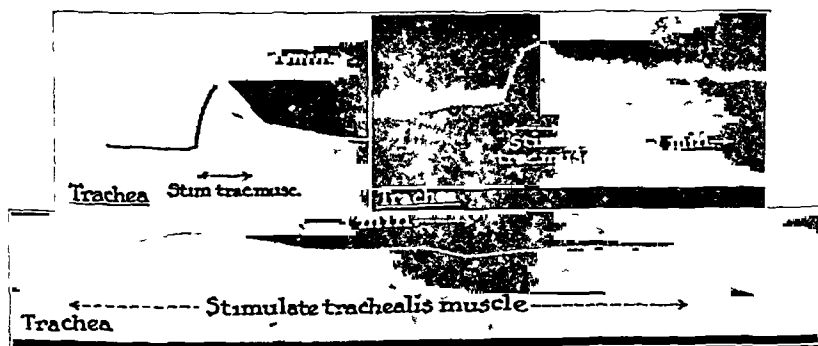


Fig 3—The two upper tracings represent the response to stimulation of the trachealis muscle in 2 different dogs (The tambour was connected with a balloon in the trachea) In each instance the stimulus was maintained for about fifteen seconds Note that contraction persisted after cessation of the stimulus The lower curve represents the response obtained by stimulation maintained for three and one-half minutes There was a surprising lack of fatigue as determined by the maintenance of the height of the curve However when the stimulus was removed there was a rather sharp drop to the normal level

that reason young dogs must be used for such experiments on the trachea

When the pararecurrent or vagus nerve was stimulated there was likewise a contraction of the trachealis muscle (fig 5) but naturally not as pronounced as when the muscle was stimulated directly On certain occasions irritation of the trachea as produced by scratching the surface with a needle will produce a contraction but it should be emphasized that this response is obtained only occasionally It appears to be more readily obtained when the anesthesia is light As a matter of

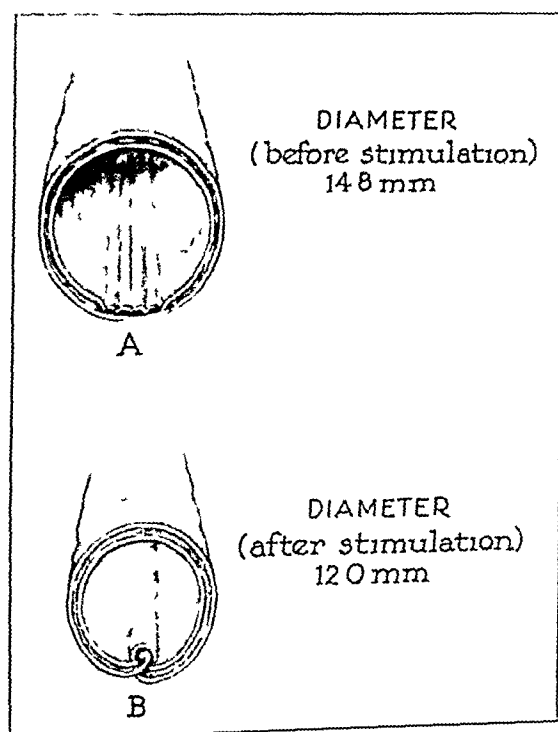


Fig 4—*A*, drawing of a dog's trachea, showing the slightly wrinkled trachealis muscle. *B*, drawing of same trachea while the muscle was being stimulated. Note that the muscle has contracted into a bundle, approximating (in this instance) the ends of the cartilaginous rings. The diameter changed from 14.8 to 12 mm. Contraction of this degree is obtainable only in young dogs.

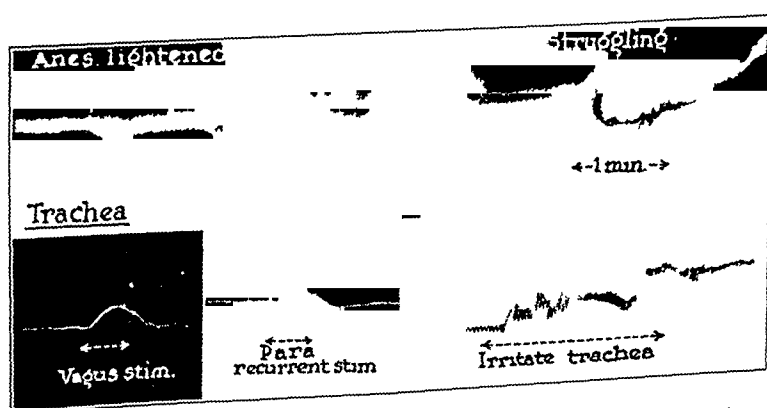


Fig 5—As anesthesia is lightened a marked fluctuation in tonus of the trachealis muscle (in the dog) is noted, with a tendency toward an increasing amount of spasm up to its maximum capacity. Electric stimulation of the vagus and the pararecurrent nerves produces contraction of the trachealis muscle, as would be expected. Likewise irritation of the trachea (scratching with a needle) produced a marked spasm, but this result is obtained only occasionally and is no doubt greatly dependent on the depth of anesthesia, being more active under light anesthesia.

tact changing the depths of anesthesia without an additional stimulus will invariably result in a marked change in the size of the tracheal lumen. The most constant change is constriction of the trachea during the period when the anesthesia is being lightened. With the balloon in the larynx, spasm of the vocal cords can likewise be demonstrated during fluctuations in depth of anesthesia, particularly when the anesthesia is lightened (fig. 8).

As would be expected with the balloon in the larynx, crushing the recurrent nerve resulted in laryngeal constriction (fig. 6), presumably the tonus of the cricothyroid muscle (innervated by the superior laryngeal nerve) with consequent adduction of the vocal cord is the factor producing the constriction. Manipulation of the nerve produced a

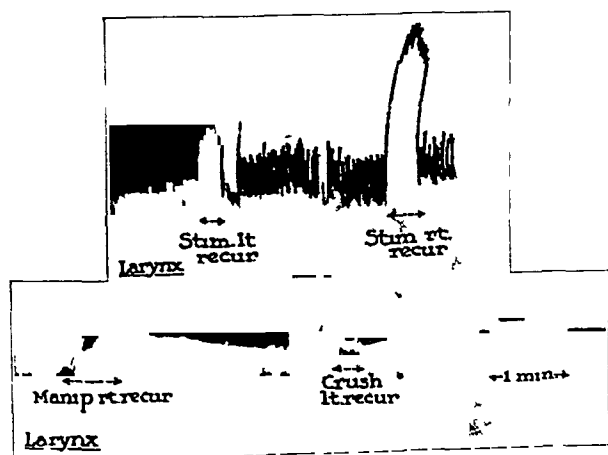


Fig. 6—With the balloon in the larynx, electric stimulation of the recurrent nerve, under usual circumstances, produces a bilateral adductor (see text) spasm. In this experiment manipulation induced a mild adductor spasm and crushing the nerve a more pronounced spasm, as would be expected. Crushing the recurrent nerve paralyzes it, thus affecting the adductor as well as abductor fibers within it and allowing the cricothyroid muscle, which is innervated by the superior laryngeal nerve, to adduct the cord by its tensor action. It is obvious then that if any effect is produced most types of stimulation or trauma are likely to result in an adductor spasm.

spasm of less intensity. This response is by no means constant and is only mild. It has been observed in human beings by laryngoscopic examination (Curtis¹¹). However, during manipulation of the nerve incident to total thyroidectomy, Seed¹² has not noted sufficient adductor spasm.

¹¹ Curtis, G. Personal communication to the author.

¹² Seed, L. Personal communication to the author.

to produce stridor. Stimulation of the recurrent nerve results primarily in adduction of the cords, but circumstances may occasionally result in abduction. This seemingly paradoxical reaction is made possible by the fact that the nerve contains abductor as well as adductor fibers (Russett¹³), then threshold of response to stimuli appears to be variable. The sharp adductor spasm which is so commonly obtained has been noted by numerous observers and may involve both cords. Fishman¹³ showed experimentally that the bilateral action was peripheral as well as central by obtaining the same response (bilateral spasm) under stimulation of one recurrent nerve when the other was severed. He remarked that this did not necessarily prove that there was a chiasmatic innervation but was of the opinion that the stimuli reached the other side by crossing nerve fibers of peripheral synapses. The strong adductor action proves that the adductor muscles, at least in this instance, were stronger

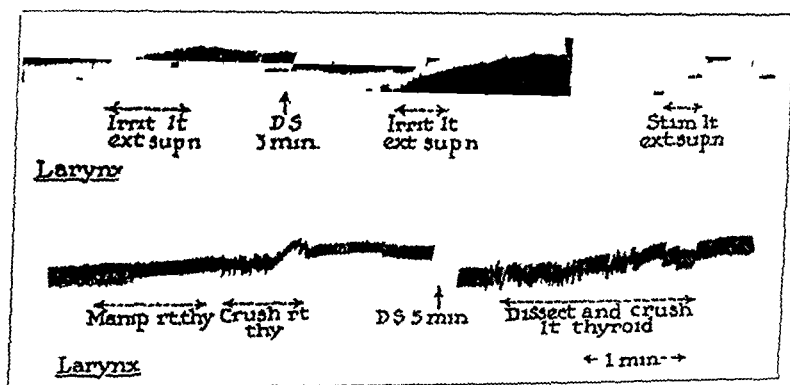


Fig 7—Irritation of the external superior laryngeal nerve usually produces a mild adductor spasm of the cords. In this experiment the drum was stopped for three minutes (indicated by D S) to allow the nerve and muscles to recover. Electric stimulation of the nerve likewise results in adductor spasm. In this experiment manipulation and crushing the thyroid produced an adductor spasm. However, this response is by no means constant and apparently occurs in the animal only when the anesthesia is light.

than the abductor, or that the cricothyroid muscles, which are innervated by the superior laryngeal nerve, were stimulated by reflex or by an overflow of stimuli.

Irritation and stimulation of the external superior laryngeal nerve produce laryngeal constriction (fig 7). Manipulation and crushing of the thyroid may produce no demonstrable effect on the tonus of the laryngeal muscles, but occasionally (fig 7) a definite laryngeal constriction is produced. This result is, of course, comparable to the

13 Fishman, L. Z. Personal communication to the author.

adductor spasm which is occasionally noted during thyroidectomy when clamps are applied to certain parts of the thyroid even though this area is a considerable distance from the recurrent nerve itself. The action is undoubtedly reflex.

As stated previously conflicting results are occasionally obtained, and since the early work of Semon and Hooper they have been the subject of much dispute. The sharp relaxation of the cords demonstrated in figure 8 by traumatizing the trachea (crushing the edge with a hemostat) is an example of an inconsistent result. There appears to be no decisive explanation.

COMMENT

An analysis of the experiments reveals that the trachealis muscle (at least in the dog) is capable of a definite contraction. Stimulation of

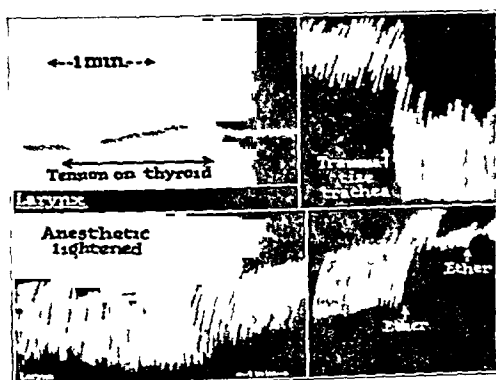


Fig 8—Occasionally tension on the thyroid will produce an adductor spasm of the vocal cords. The sharp abductor response obtained by traumatizing the dog's trachea (crushing the edge with a hemostat) appears paradoxical, abductor response of this type was obtained rarely in the experiments performed in this report. The adductor spasm produced by lightening the anesthetic or by suddenly increasing the amount of ether given is a response well known to all.

the muscle itself produces a greater contraction than stimulation of the pararecurrent nerve but to a degree which decreases the diameter of the trachea no more than 2.5 or 3 mm. The contraction produced by reflex stimuli did not approach this in intensity except perhaps during the struggling incident to a lightening of the anesthetic. A narrowing of the trachea to a degree greater than that mentioned is prevented by contact of the tip of the cartilaginous rings and by the support afforded by the horseshoe-shaped rings themselves. Obviously if through abnormality of some type or other the support of the rings is lost an

actual collapse would be possible Colp and Louria¹⁴ found that resection of at least seven rings was necessary in dogs before an obstructive collapse was produced In the human being the cartilaginous support may be lost either through constitutional disease or through pressure atrophy produced by an adenoma of the thyroid The elasticity of the trachea minimizes the effect of pressure by an adjacent nodule of thyroid but numerous proved instances of tracheal collapse of this type have been reported (Peterson and Rovenstine,¹⁵ Henry,¹⁶ Moersch¹⁷ and others) The patient reported on by Moersch had stridor immediately after operation, but tracheotomy was not necessary until the fourth postoperative day Bronchoscopic examination revealed an absence of tracheal rings and collapse of the lateral walls of the trachea Every one is acquainted with the serious obstructive effect of a postoperative hemorrhage Even after evacuation of the blood clot there may be sufficient edema and infiltration of the mucous membrane to make tracheotomy necessary, as has been noted by Rosenblatt¹⁸

Additional experiments were carried on to determine whether or not the negative pressure developed in the respiratory passages by forced inspiration in the presence of a laryngeal obstruction might produce occlusion of the trachea The trachea and larynx were removed from 10 patients at autopsy and the trachea was subjected to a negative pressure of 70 mm of mercury In one instance there was complete collapse of the tracheal wall at a negative pressure as low as 20 mm of mercury (fig 9A) This patient died of pancreatic asthenia and pronounced fatty infiltration of the liver, the disease process was probably instrumental in the loss of the normal stiffness in the cartilaginous rings In no other instance did such a pronounced collapse of the trachea take place in my experiments with negative pressure, in fact, the average decrease in the lateral diameter when the interior of the trachea was subjected to a negative pressure of 70 mm of mercury was only 3 mm Macleod¹⁹ gives 100 mm of mercury as the maximum positive pressure developed during forced expiration and 70 mm of mercury as the negative pressure during forced inspiration For that reason no

14 Colp, R., and Louria, H. W. Dyspnea Following Thyroid Operation, *Arch Surg* **11** 200 (Aug) 1925

15 Peterson, M. C., and Rovenstine, E. A. Tracheal Collapse Complicating Thyroidectomy, *Anesth & Analg* **15** 300, 1936

16 Henry, C. K. P. Tracheal Collapse During Thyroidectomy, *Anesth & Analg* **6** 146, 1927

17 Moersch, H. J. Tracheal and Esophageal Compression as a Result of Adenomatous Goiter, *Ann Otol, Rhin & Laryng* **40** 909, 1931

18 Rosenblatt, M. S. Tracheotomy After Thyroidectomy, *Northwest Med* **28** 330, 1929

19 Macleod, J. J. R. *Physiology in Modern Medicine* St Louis, C. V. Mosby Company, 1930

negative pressures greater than 90 mm of mercury were used. It is possible that if a spasm of the trachealis muscle were present a greater narrowing of the trachea would be possible but the resistance of the rings would prevent total collapse unless atrophy of the rings were present. In fact it is probable that a more pronounced obliteration of the lumen of the trachea would result if it were submitted to a negative pressure of forced inspiration with the larynx blocked and with the trachealis muscle relaxed so that it could protrude anteriorly into the lumen as shown in figure 9A.

During the course of the preceding experiments it was noted that the stimuli producing a spasm of the adductor muscles of the larynx or of the trachealis muscle were similar. In fact there was a decided

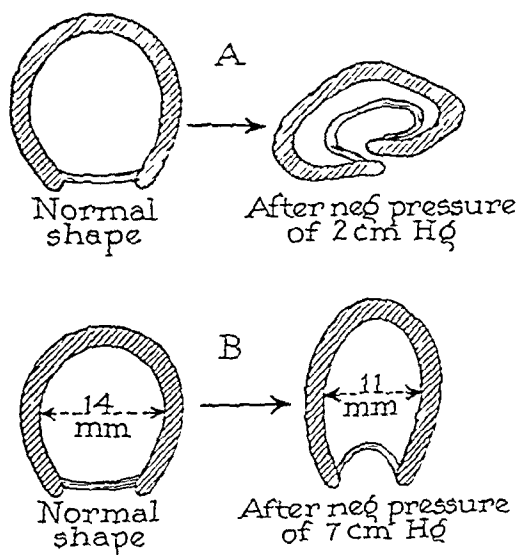


Fig 9—A represents an almost total collapse of the trachea (of a human being) as produced by a negative pressure of 2 cm of mercury in a trachea removed at autopsy. This amount of collapse is uncommon. The patient died of pancreatic asthenia and fatty degeneration of the liver. The tracheal rings were undoubtedly abnormal so far as they had lost their normal support. B represents the average influence of a pressure of -7 cm of mercury on 9 other tracheas removed at autopsy from patients dying from various causes. The diameter has been narrowed only 3 mm.

tendency for the spasm to effect the trachea and the larynx simultaneously. The larynx is more susceptible and naturally muscular spasms involving it are more important than changes in the trachea particularly since complete collapse of the trachea is not possible in a normal trachea and since in spasm of the larynx the adductors predominate, thereby producing obstruction. It was found that various

stimuli, such as crushing or manipulation of the thyroid or irritation of the trachea or recurrent laryngeal nerves, would produce adductor spasm. It is probable that in many instances the obstruction is produced by spasm of the adductors, whereas in other instances the adductor action is produced solely by muscle tonus in the presence of paralysis of the abductors. The tendency of the abductors to become paralyzed long before the adductors as the result of mild trauma (Semm's law) has been supported by many observers. This simple phenomenon in certain instances might explain the predominance of the adductors over the abductors in the case of trauma. However, in many instances the adduction of the vocal cords is no doubt primarily a reflex resulting from stimulation by irritation or trauma, in this instance the adductors as well as the abductors might be stimulated but the more powerful adductors would control the action of the cords. When this reflex stimulation takes place the resultant effect would likewise be likely to be bilateral. This effect on both sides as stated previously, is thought to be produced through a direct crossing of stimuli at the periphery (i. e. within the larynx) and, as Fishman has emphasized, may not be the result of another reflex of central origin.

One of the most pronounced spasms noted during the course of the experiments described was observed when the femoral vein was isolated preparatory to an intravenous injection. The trauma incident to the isolation of the vein, consuming perhaps five or ten seconds, was the inciting factor.

The causes of adductor spasm of the larynx as noted clinically are too numerous to attempt to enumerate. Paralyzes occurring as long as several weeks or months after thyroidectomy, presumably through the action of compression of the nerve by scar, have been reported. More commonly this delayed reaction is noted a few hours or a day or two after operation and in such instances is produced by excessive edema of the structures surrounding the recurrent nerve or by infiltration of that area by blood, thereby resulting in compression of the nerve. Several years ago I observed a patient with a large substernal goiter who was able to talk normally for twelve hours after thyroidectomy, but serious stridor gradually developed until tracheotomy was necessary twenty-four hours after operation. At the time of the tracheotomy a hemorrhage into the tissues on the floor of the operative field on each side was noted, but little blood clot was present in the wound itself. In this instance it appears likely that the infiltration of the tissues in the floor of the operative field had involved the recurrent nerve on each side, thereby resulting in paralysis of the vocal cords with consequent laryngeal obstruction.

The paralyzes described in the foregoing paragraph may be considered as being mechanical in origin. However, temporary paralyzes

of reflex origin are much more common. Anesthetists are aware of the frequency of laryngeal spasm and look on it as being one of the most important obstacles in obtaining smooth anesthetics. In fact some anesthetists (Sise²⁰ and others) feel that laryngeal spasm is so troublesome that they use intratracheal anesthesia for laparotomies and similar operations so that closure of the glottis cannot take place. Brewer²¹ and his associates showed experimentally that traction on the mesentery or stimulation of the splanchnic nerve with the faradic current resulted in cessation of breathing with closure of the glottis by adductor spasm of the vocal cords. They offered additional proof of this reflex effect by obtaining action potentials from one of the recurrent laryngeal nerves while visceral traction or electric stimulation was performed.

SUMMARY

After consideration of the problem it was concluded that the obstruction to respiration as sustained by the patient described in this report resulted from reflex closure of the glottis (adductor spasm approximating the vocal cords). The stimulus producing this action may have been produced by the application of clamps on the capsule of the gland or by pulling on the thyroid lobe which may or may not have resulted in tension on the recurrent laryngeal nerve on that side. The spasm undoubtedly involved both sides. Experimental support for these explanations are presented. The fact that the patient recovered on the operating table without any hemostats being removed from the region of the nerve would appear to prove that actual trauma to the nerve had nothing to do with the action unless it was tension on the nerve.

The trachealis muscle is capable of considerable contraction either by direct stimulation or by reflex action. The elastic resistance of the cartilaginous bars prevents a decrease in diameter of more than 3 mm unless an erosion of the rings is present (as may be produced by compression from an adenoma of the thyroid) or a loss in strength of the rings is created by constitutional disease. True complete tracheal collapse therefore cannot occur in a normal human trachea.

The decrease in diameter of the trachea as observed in the operation mentioned could be explained on the basis of a spasm of the trachealis muscle or a partial collapse incident to obstruction produced by adductor laryngeal spasm or both. The latter factor would appear to be more

²⁰ Sise, L. F. Choice of Anesthesia for Surgery of the Upper Abdomen. *Am J Surg* 40 22, 1938.

²¹ Brewer, N., Luckhardt, A. B., Lees, W. M. and Bryant, D. S. Reflex Closure of the Glottis by Stimulation of Afferent (Visceral) Fibers. *Anesth & Analg* 13 257, 1934. Brewer, N., and Bryant, D. S. The Role of the Splanchnics in the Adductor Spasm of the Vocal Cords Following Visceral Traction. *ibid* 14 190, 1935.

significant. This amount of change in size of the caliber of the trachea is undoubtedly rare as a complication of thyroidectomy.

Obstruction created by adductor spasm of the larynx with approximation of the cords is a much more significant cause of respiratory difficulty than obstruction in the trachea not only during thyroidectomy but during most other operations as well. This spasm is reflex and can be produced experimentally by such methods as tension on the thyroid, crushing and manipulation of the thyroid, trauma to blood vessels, lightening of anesthesia or sudden administration of an anesthetic (ether). Most of the reflex obstructions produced experimentally by the aforementioned methods are obtained only occasionally and in that respect resemble clinical experiences.

Undoubtedly, the fact that the recurrent nerve contains adductor and abductor fibers, as pointed out by Russel,⁸ is of considerable assistance in explaining why various stimuli (whether reflex or otherwise) result so commonly in adductor spasm of the larynx, particularly since the adductor muscles are obviously much stronger than the abductor. The nerve fibers going to the abductors of the larynx are larger than those going to the adductor.⁷ Although large fibers are more excitable²² than smaller fibers, by the recognized neurologic principles they should likewise be less resistant to trauma. The fact that the abductor muscles lose their power to respond to electric stimulation before the adductor, as determined at autopsy on human beings²³ and by experiments on the excised larynx of the dog²⁴ would likewise be of significance in explaining why adductor action results so commonly in the laboratory and operating room when trauma serves as the source of the stimuli.

Experiments described in this report indicate that the respiratory obstruction sustained by the patient herein reported on what was caused by reflex adductor spasm of the larynx. A large proportion of tracheotomies performed for respiratory obstruction during thyroidectomy are done for this condition. Proof of this statement will be at hand if it is possible to remove the tracheotomy tube within a day or two after tracheotomy.

If significant respiratory stridor is encountered when the surgeon is positive that the recurrent nerve has not been injured, he should immediately stop the operation, release all tension on the thyroid and remove any pressure such as might be inflicted by weight of hemostats. Tracheotomy is naturally to be avoided as far as possible, particularly

²² Gerard, R. W. Nerve Conduction in Relation to Nerve Structure, *Quart Rev Biol* 6 59, 1931

²³ Jeanselme, D., and Lermoyez, M. Etude sur la contractilité post mortem et sur l'action de certains muscles, d'après des expériences faites sur des cadavres de cholériques, *Arch de physiol norm et path* 6 109, 1885

²⁴ Lemere⁷ Semon and Horsley¹⁰

since the entire wound in such instances usually becomes infected. The insertion of a catheter through the larynx into the trachea will obviously combat the obstruction effectively. In such instances it may be impossible to remove an intratracheal catheter or tracheotomy tube for several days.

The depth of anesthesia is undoubtedly important in the causation and treatment of laryngeal spasm. In the first place it will occur much less frequently under local anesthesia. If the patient is anesthetized deeply before the operation is begun laryngeal spasm will be much less likely to develop. If stridor develops during the operation, for which light anesthesia is being used, putting the patient into a deeper stage of anesthesia will usually correct it but rarely so unless the operator ceases all manipulation. On numerous occasions, however, deepening the anesthesia will be of no avail, moreover, if the stridor is severe and develops rapidly, the anesthetist will probably be fearful of any attempt to deepen it. Regardless of whether the anesthesia is lightened or deepened in an attempt to control the stridor, it will obviously be necessary to administer a mixture high in oxygen content. As pointed out by Lahey²⁵ helium should always be administered with the oxygen because of its effect of increasing the flow of oxygen through the narrowed glottic aperture.

It must of course be appreciated that an actual mechanical obstruction of the trachea may be produced during thyroidectomy by careless manipulation of the thyroid lobes, particularly if they are large and extend posteriorly. If a softening or atrophy of several tracheal rings has taken place because of compression by an adenoma, no amount of care may prevent obstruction at this point because of collapse of the walls of the trachea.

²⁵ Lahey, F. Modern Development in Anesthesia and Anesthetists, South M. J. 31, 29, 1938.

TUMOR OF THE HYPOPHYSIAL DUCT (RATHKE'S CYSTS)

REPORT OF ELEVEN CONSECUTIVE CASES

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A congenital tumor arising from an embryologic rest in the region of the pituitary body and the sella turcica is rarely encountered even in a large neurosurgical clinic, but the occurrence is sufficiently frequent to warrant consideration of such a tumor in the differential diagnosis of the cause of disturbance of vision in a child or a young adult. Particularly is this true if the patient's vision cannot be improved with corrective lenses or if there is edema of the optic disks as observed on fundusoscopic examination. The diagnosis of a tumor in the chiasmal region usually is not difficult if the condition is considered as a possibility.

Cases of intracranial tumor arising from a residual cell rest of the primitive hypophyseal duct were reported as early as the latter part of the nineteenth century. The early reports were based on both operative material and material obtained at necropsy. In spite of the excellent anatomic, pathologic and clinical studies which have been derived from such sources, adequate attention has not been paid to the surgical problem presented by cases of this type.

This report is based on a careful analysis of the records of 11 consecutive cases in which the clinical diagnosis was verified surgically and in which there was neither operative nor subsequent mortality¹. The patients were operated on by one surgeon (J G L), and this explains the small number of patients with this type of tumor seen in such a relatively long period. Cases in which this type of tumor was observed by Adson and Craig during the same period (April 1935 to Jan 28, 1938) were not included in this study. In view of the unusually fortu-

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1 One patient was killed in an automobile accident one and one-half years after operation

nate results both operative and postoperative this series of cases was considered important enough to be subjected to critical study in an effort to determine what measures were undertaken which might influence the mortality rate in cases of this serious intracranial lesion. Lesions of the hypophyseal duct are the source of one of the most formidable challenges presented by tumors involving the central nervous system.

The acquisition of knowledge as to the exact mode of origin of the hypophysis cerebri and as to the significance of the squamous epithelial cell rests from which tumor of the hypophyseal duct arises has been slow and tedious. Rathke² in 1838 was the first to assert that the pituitary body developed from a diverticulum of the pharynx. Some years later (1857) Zenker³ observed squamous epithelial cysts in the region of the optic chiasm but did not fully appreciate their significance or their importance in the production of intracranial tumor.

The relative rarity of tumor of the hypophyseal duct is illustrated by the infrequency of reports of cases of this lesion. The high operative mortality probably accounts to some extent for the scarcity of articles on the subject. Up to 1916 when Jackson⁴ reported a collected series of 38 cases of tumor arising from remnants of the hypophyseal duct reports of cases had appeared sporadically and had been based almost entirely on postmortem material. Duff⁵ in 1920 was able to add 18 cases gathered chiefly from a more careful perusal of the literature thus bringing the number of reported authentic cases at that time to the rather small total of 56.

Since that date, tumors of this type have been observed and reported with much greater frequency nevertheless they continue to represent a very small percentage of chiasmal tumors and constitute a group worthy of intensive study especially from the standpoint of proper surgical management.

In the past as at the present time much confusion was evident in regard to the proper designation of this type of tumor. It has been described under a great variety of names depending apparently on the personal points of view and interests of the authors. Histologically it has been classified as adamantinoma anatomically as interpeduncular or suprasellar cyst and embryologically as Rathke's cyst craniopharyn-

2 Rathke cited by von Mikulicovic, V. Wirbelsaite und Hirnanhang Arch f mikr Anat **11** 389-441 1875

3 Zenker cited by Erdheim, I. Pathologie der Hypophysengechwülste Ergebn d allg Path u path Anat **21** 482-561 1926

4 Jackson, H. Craniopharyngeal Duct Tumors J A M A **66** 1082-1084 (April 8) 1916

5 Duff, W. C. Hypophyseal Duct Tumors. A Report of Three Cases and a Fourth Case of Cyst of Rathke's Pouch Ann Surg **72** 537-555 (Nov.) 725-757 (Dec.) 1920

glioma and tumor of the hypophysial duct. As will be shown later, it may vary greatly in its gross and histologic appearance as well as in its exact situation. However, all instances have in common the development from squamous epithelial cell rests which are remnants of the embryonic hypophysial duct, and consequently it appears logical to designate such a growth as a tumor of the hypophysial duct.

EMBRYOLOGY

The hypophysis cerebri is developed by the union of two portions, one an outpouching of the wall of the third ventricle, forming the neural posterior lobe, the other an outpouching from the *Rachenepithelium* of the primitive buccal cavity, forming the glandular anterior lobe.

The history of the development of the pituitary body makes a most interesting chapter in embryology, the details of which are vital to a clear understanding of the problem of tumor of the hypophysial duct. Muller⁶ in 1871 and Mihalkovics⁷ in 1875 are generally given credit for having first presented accurate and complete descriptions of the intricate embryonic mechanism⁸ whereby the adult pituitary body develops from the primitive buccal cavity⁹.

6 Muller, W, cited by Atwell^{9a}

7 von Mihalkovics, V. Wirbelsaite und Hirnanhang, Arch f mikr Anat **11** 389-441, 1875

8 For a more detailed embryologic description, one may consult the thesis submitted to the University of Minnesota by Dr C Hunter Shelden.

9 (a) Atwell, W J. The Development of the Hypophysis Cerebri of the Rabbit (*Lepus Cuniculus* L.), Am J Anat **24** 271-337 (Sept.) 1918. (b) Carmichael, H T. Squamous Epithelial Rests in the Hypophysis Cerebri, Arch Neurol & Psychiat **26** 966-975 (Nov.) 1931. (c) Erdheim, J. Pathologie der Hypophysengeschwulste, Ergebn d allg Path u path Anat **21** 482-561, 1926. (d) Frazier, C H, and Alpers, B J. Tumors of Rathke's Cleft (Hitherto Called Tumors of Rathke's Pouch), Arch Neurol & Psychiat **32** 973-984 (Nov.) 1934. (e) Goette, cited by Duffy⁵. (f) Harbitz, F. Tumours Arising from the Hypophyseal Duct, and Other Neoplasms Related Thereto, Chordomas, Acta path et microbiol Scandinav **12** 38-78, 1935. (g) Kiyono, H. Ueber das Vorkommen von Plattenepithelherden in der Hypophyse, Virchows Arch f path Anat **252** 118-145, 1924. (h) Luschka, cited by Atwell^{9a}. (i) McLean, A J. Die Cramopharyngealtaschentumoren (Embryologie, Histologie, Diagnose und Therapie), Ztschr f d ges Neurol u Psychiat **126** 639-682, 1930. (j) Raschussen, A T. Ciliated Epithelium and Mucus-Secreting Cells in the Human Hypophysis, Anat Rec **41** 273-282 (Feb.) 1929. (k) Susman, W. Embryonic Epithelial Rests in the Pituitary, Brit J Surg **19** 571-576 (April) 1932. (l) Tilney, F. An Analysis of the Juxta-Neural Epithelial Portion of the Hypophysis Cerebri, with an Embryological and Histological Account of a Hitherto Undescribed Part of the Organ, Internat Monatschr f Anat u Physiol **30** 258-293 1914. (m) Waterston, D. The Development of the Hypophysis Cerebri in Man with a Note upon Its Structure in the Human Adult, Tr Roy Soc Edinburgh **55** 125-145 (May 20) 1927. (n) Ewing, J. Neoplastic Diseases ed 2, Philadelphia, W B Saunders Company, 1922.

SITUATION

On theoretic grounds alone one might expect to find that tumor of the hypophyseal duct develops at any point along the course of the primitive hypophyseal duct however, clinically it is rarely found extracranially. Frequently typical groups of cell rests have been found in the region of the vomer and the sphenoid sinus, but they apparently do not result in the formation of a tumor or if they do they do not produce symptoms. The favorite site of origin of tumor of the hypophyseal duct is in the midline above the sella turcica in the infundibular region along the hypophyseal stalk or beneath the optic chiasm. It may develop either above or below the diaphragm or dural roof of the sella, however, in many instances it produces early rupture of this membrane, and then accurate anatomic localization may be impossible¹⁰. Thus, it is seen that the tumor develops most frequently from the region of the infundibulum and from the anterior superior aspect of the capsule of the anterior lobe of the pituitary body, a site which corresponds to that at which epithelial cell rests are found in a high percentage of normal¹¹ pituitary bodies.

GROSS APPEARANCE

Tumor of the hypophyseal duct varies in gross appearance from a small, solid, well circumscribed, discrete growth to a huge, multilocular cyst producing marked displacement of the adjacent structures. The capsule is in many instances smooth and white and of sufficient density to tolerate considerable manipulation without tearing, however, it may be thin and fragile and may have a dark appearance as a result of the color of the contained fluid¹². If the tumor is of long standing or has developed with great rapidity it may infiltrate the surrounding tissue to such an extent that surgical dissection of the lesion from the adjacent structures is impossible. Although the tumor is generally solid in its early stages, it soon undergoes cystic degeneration, the fluid content of the cyst is usually yellowish, dark brown or greenish brown, and there often is as much as 2 to 3 ounces (60 to 90 cc) of this fluid. Generally, the fluid contains crystals of cholesterol which are clearly visible floating on the fluid as the cystic cavity is opened. Calcification is usually present

10 Cushing, H. Intracranial Tumors. Springfield, Ill., Charles C. Thomas, Publisher, 1932.

11 Bartels, P. Ueber die Beziehungen von Veränderungen der Hypophysengegend zu Misswachstum und Genitalstörungen (Dystrophia adiposo-genitalis), *München med Wchnschr* 55 201-202 (Jan 28) 1908.

12 Dandy, W. E. The Brain, in Lewis, D. Practice of Surgery. Hagerstown Md. W. F. Prior Company, Inc. 1932 pp 598 605.

in the lesion and is said by some authors to be demonstrable roentgenographically in 85 per cent of cases¹³. The amount of calcium present may vary from that which produces minute local areas of calcification above the sella turcica to that which produces a definite line of calcification completely outlining the entire extent of the tumor (fig 1). Extreme degrees of calcification (fig 2) have been reported, in which the entire tumor became stony hard, so that it was impossible to section it by routine methods for microscopic studies¹⁴.

HISTOLOGIC APPEARANCE

The microscopic appearance of tumor of the hypophysial duct is as variable as the gross appearance¹⁵. The criterion for diagnosis, accord-



Fig 1 (case 5) —Lateral roentgenogram of the head, showing diffuse calcification in the midline at the outlet of the sella turcica and partial destruction of the dorsum sellae

ing to Critchley and Ironside,¹⁶ is the presence of a single row of columnar cells which correspond in structure to the embryonic ameloblasts and which are arranged in palisade formation at the periphery of the epithelial masses

13 McKenzie, K. G., and Sosman, M. C. The Roentgenological Diagnosis of Craniopharyngeal Pouch Tumors, *Am J Roentgenol* **11** 171-176 (Feb) 1924

14 Bailey, P. Note Concerning Keratin and Keratohyalin in Tumors of the Hypophyseal Duct, *Ann Surg* **74** 501-505 (Oct) 1921

15 Frazier, C. H., and Alpers, B. J. Adamantinoma of the Craniopharyngeal Duct, *Arch Neurol & Psychiat* **26** 905-965 (Nov) 1931

16 Critchley, M., and Ironside, R. N. The Pituitary Adamantinoma. *Brain* **49** 437-481 (Dec) 1926

The outer row of cells lying on a basement membrane is the most constant histologic feature. These cells are long and slender, they have oval elongated deeply stained nuclei and are so situated that the long axis of each is approximately at right angles to the underlying basement membrane¹⁶ (fig 3)

The intermediate zone is generally less distinct than the outer zone and frequently is absent. The cells which constitute this area are roughly similar to those of the peripheral zone but are less elongated and less uniform in appearance.

The innermost area of the epithelial masses constitutes the stellate zone. This portion of the epithelial column appears as a fine cobweb-like reticulum in which are enmeshed scattered, loosely arranged cells.

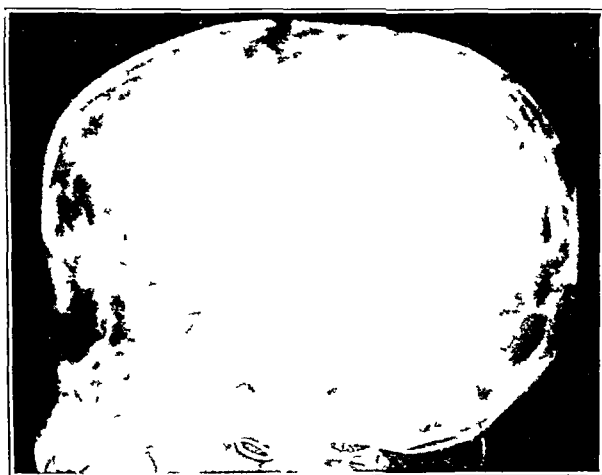


Fig 2—Lateral roentgenogram of the head of a 7 year old child, showing an extreme degree of calcification in what was considered to be a tumor of the hypophyseal duct. The child was blind but had no other symptoms at the time of examination. In addition to the erosion of the sella turcica one may note the separation of the cranial sutures and the erosion of the calvarium secondary to increased intracranial pressure.

They stain less intensely than the closely packed peripheral columnar layer of cells and the nuclei which are large and vesicular, frequently have a crescentic arrangement. This formation is often seen within the epithelial whorls commonly encountered in the stellate zone. The whorls closely simulate those characteristically found in squamous cell epithelium. The central portions of these whorls probably undergo hyalinization or keratinization and later calcification which accounts for the frequent presence of masses of calcium in the central areas of the whorls. Generally the stroma or supporting structure is fibrous tissue.

arranged irregularly among the epithelial columns. However, the pattern is dominated by two rather constant types. In one the fibrous tissue is present as fine strands with a lacelike appearance. The other type consists of coarse, dense fibrous tissue with narrow slitlike interspaces.

Occasionally the epithelial masses are completely surrounded by neuroglia and sometimes neuroglia is completely absent. Usually, examination of the glial tissue does not reveal any histologic evidence of reaction to the growth of the adjacent tumor.

Degeneration associated with cyst formation is a conspicuous feature of tumor of the hypophysial duct. In addition to true cysts, there are



Fig 3—Palisade formation of the elongated columnar cells forming the ameloblast layer, a definite basement membrane is demonstrated, the specimen is stained with hematoxylin and eosin ($\times 450$)

numerous slits or prism-shaped empty spaces, which represent former sites of cholesterol crystals in the tissue. Fresh sections examined under the polariscope reveal these refractile crystals.¹⁷ Bailey¹⁸ said that calcium is visible microscopically in every tumor of the hypophysial duct. In our cases the area of calcification varied in size from minute,

¹⁷ Footnote deleted by authors

¹⁸ Bailey, P. Intracranial Tumors, Springfield, Ill., Charles C Thomas, Publisher, 1933

discrete particles to large irregular calcified masses. About the cholesterol crystals and masses of calcium large foreign body giant cells not infrequently are seen.

Intercellular bridges are common in fresh sections stained by the polychrome methylene blue method. Keratohyaline granules frequently have been reported in tumor of the hypophyseal duct¹⁴ but such granules were not observed in this series of cases.

A striking feature of the histologic appearance of the tumor is its extreme avascularity. This may in part account for the readiness with which the tumor undergoes diffuse degeneration, with cyst formation.

The presence of visible bone in sections of the tumors has been reported consistently in the literature. In spite of a careful search, no such material was observed in this particular series.

CHARACTERISTIC PATHOLOGIC CHANGES

Tumor of the hypophyseal duct must be distinguished from several closely related but histologically dissimilar tumors of embryonic origin. Dermoid and epidermoid tumor not infrequently occur adjacent to the sella turcica, when either tumor occurs above the tentorium cerebelli the origin usually is in the basofrontal region. An epidermoid tumor is one in which only squamous and basal epithelium are present. A tumor which, in addition, contains other elements of normal skin such as sweat glands, sebaceous glands or hair follicles is considered a dermoid tumor.¹⁹

Histologically the criterion for diagnosis of an epidermoid tumor is the demonstration of definite squamous epithelium. Keratohyaline granules, intercellular bridges and cornification are prominent features. In fact, it is the desquamation of the cornified cells which produces the main bulk of the contents of these cysts. When other elements of normal skin are present in addition to the squamous epithelium, the tumor is a dermoid. On rare occasions all three germ layers may be represented in the same tumor which is classified as a teratoma.

SYMPTOMS

In cases of tumor of the hypophyseal duct as in cases of any other lesion presenting such a wide and bizarre range of gross characteristics, the symptoms do not follow a stereotyped pattern but depend on the size and rate of growth of the tumor as well as on the order in which the adjacent structures are involved.

¹⁹ Love I. G. and Kernohan J. W. Dermoid and Epidermoid Tumors (Cholesteatomas) of the Central Nervous System. *J. A. M. A.* **107** 1876-1883 (Dec. 5) 1936.

Importance has been placed on the exact site of origin of the tumor in relation to the dural roof of the sella turcica as a determining factor in the developmental sequence of the clinical symptoms.²⁰ A tumor which develops from epithelial cell rests situated below the diaphragma sellae naturally compresses first the pituitary body and later extends upward to involve the cephalad structures. As this type of lesion expands upward it must push the dural roof before it, hence, signs of pituitary dysfunction may long antedate other symptoms. Such a lesion, because of its anatomic situation, may be considered an epidural growth, and it has been suggested²⁰ that in many instances long-standing mild headache may be the result of gradual upward stretching of this portion of the dura rather than a low grade hydrocephalus.

A tumor arising above the dural roof of the sella turcica has its origin in cell rests situated along the stalk of the infundibulum and the anterior superior aspect of the capsule of the pituitary body. Naturally, such a growth is within the subarachnoid space, and it early tends to fill the cisterna basalis. A tumor of this type tends to produce early involvement of the visual pathways and of the hypothalamus, whereas the element of pituitary dysfunction is not marked, because the lesion is separated from the pituitary body by the diaphragma sellae.

If the tumor originates from rests situated at the point of passage of the stalk through the dural roof, rapid growth of the mass may cause simultaneous functional changes in structures both above and below the diaphragma sellae.

The symptoms may be further altered from any given pattern by a sudden hemorrhage into a large cystic cavity or by a rapid local degenerative process which produces irritant material that initiates a local or diffuse inflammatory process in the suprasellar region.²⁰

The symptoms of tumor of the hypophysial duct have been described very well by Cushing.¹⁰ They may be the result of pituitary dysfunction, visual disturbance, hypothalamic compression or increased intracranial pressure associated with hydrocephalus. Generally the initial symptoms are either visual or pituitary, but if the lesion is allowed to progress to a sufficient size the majority of the classic symptoms will be present.

Pituitary involvement results in degrees of dysfunction varying from mild, easily overlooked hypopituitary states to obvious dystrophia adiposogenitalis. The endocrine disturbances are generally evidenced by the Frohlich type of physical appearance, however, the Lorain type of

²⁰ Wittermann, E. Hypophysengangtumoren und vegetative Zentren des Zwischenhirns, *Nervenarzt* 9: 441-453 (Sept.) 1936.

infantilism without adiposity occasionally is observed.¹⁴ Critchley and Ironside¹⁶ mentioned the frequency of the association of acromegaly with an intrasellar growth of this type but this is contrary to our experience. Neither acromegaly nor gigantism was observed in any of the cases in this series.

Cachexia is one of the less frequent manifestations of pituitary dysfunction, it has been observed by some authors in cases of tumor of the hypophyseal duct²² but it did not occur in any of our cases. In case 8 mild menstrual irregularity which was first noticed eight years before the patient came to the clinic was the first symptom; the subsequent amenorrhea antedated the onset of headache and vomiting by more than two years. In case 3 the patient who was a man aged 31 had noted an unusual feminine distribution of pubic hair and a pale and pasty complexion for many years. He remarked that it never had been necessary for him to shave oftener than every other day or even at longer intervals. In cases 2 and 5 there was a frank appearance of dystrophia adiposogenitalis. In 7 of the 11 cases there was evidence of pituitary dysfunction of notable degree. A constant observation was the low systolic blood pressure; the highest value was 110 mm of mercury and in 6 of the 11 cases the value for the systolic blood pressure was 90 mm of mercury or less.

Visual disturbances in our experience constituted the most common initial symptom; they were present in some form in every case. Progressive dimness of vision was the most common mode of onset and in most instances (8 of 11 cases) this was the result of gradually developing primary atrophy of the optic nerve. It is noteworthy that in 6 of these 8 cases the defect in the visual field was bitemporal. Homonymous hemianopia (fig. 4) occurred in 4 cases; in 2 there was associated mild papilledema and in 1 there was a well advanced degree of primary atrophy of the optic nerve. A high degree of choked disk (4 diopters) was noted in only 1 case; the patient being a girl aged 5 years. Because of the age of the child the visual fields could not be outlined. In 1 case (case 2) there was a history of definite visual

21 (a) Frazier C H. Pituitary Cachexia. *Arch Neurol & Psychiat* **21** 1-18 (Jan.) 1929. (b) Worster-Drought C, Dickson W E C and Archer B W C. Dyspituitarism of the Lorain Type Associated with a Pituitary Cyst Arising from Rathke's Cleft and Secondary Lesions in the Hypothalamic Region and Ventricle, *Brain* **50** 704-718 (Oct.) 1927. (c) Warthin A S. A Study of the Lipin Content of the Liver in Two Cases of Dyspituitarism. *J Lab & Clin Med* **2** 73-93 (Nov.) 1916. (d) Peet M M. Pituitary Adamantinomas. Report of Three Cases. *Arch Surg* **15** 829-854 (Dec.) 1927.

22 Beckmann J W and Kubie L S. A Clinical Study of Twenty-One Cases of Tumour of Hypophyseal Stalk. *Brain* **52** 127-170 (July) 1929. Bartels²³ Frazier²⁴

hallucinations which had been associated with uncinate attacks. Four of our 11 patients had had periods of diplopia as a result of weakness of a cranial nerve. On theoretic grounds one would expect that the visual findings would indicate the situation of the lesion with reference to the optic chiasm, as well as shed some light on the probable anlage of the tumor. Many authors have discussed at length the reason for the great variation in the results of visual examination, including ophthalmoscopic study and examination of the visual field. It has been postulated that a tumor arising from the superior cell rests produces choked disks and secondary atrophy of the optic nerve, whereas one arising from the inferior cell rests causes early, primary atrophy of the optic nerve. Without doubt this is true in many instances. However, the surgical

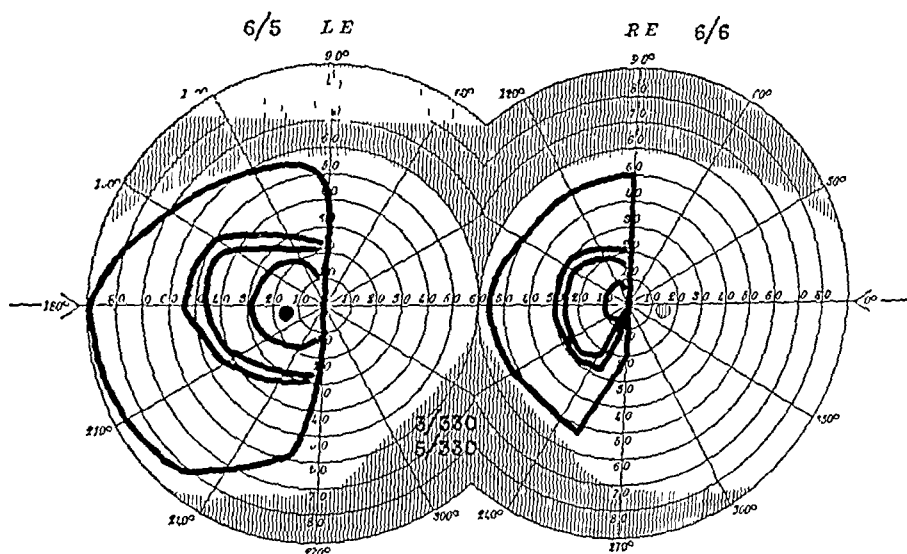


Fig 4—Preoperative visual fields in case 6, showing complete right homonymous hemianopia

findings are generally such that accurate investigation of the probable origin of the tumor is not possible. No doubt many of the variations in the visual findings can be traced further to the normal anatomic variations which occur in the position of the optic chiasm, such as variations in the outline of the sella turcica, the pituitary body and the infundibulum. The frequency with which primary atrophy of the optic nerve was associated with a bitemporal defect in the visual field is interesting and perhaps significant, it no doubt signifies a prechiasmal situation of the lesion.

Many authors have reported that hypothalamic symptoms occupy a conspicuous place in the syndrome presented by this type of tumor. However, in our series they were neither prominent nor important. Polydipsia and polyuria were not observed. Drowsiness, although

evident in 5 cases always appeared as a very late development and was probably secondary to the hydrocephalus rather than the result of primary involvement of the midbrain by the tumor

Hydrocephalus was a prominent feature, although the symptoms of increased intracranial pressure that is headache and vomiting, generally appeared late in the course of the illness. Choked disk was definite in all 3 cases in which there was no primary atrophy of the optic nerve, and in all probability choked disk would have been present in all cases had not the atrophy preceded the increase of intracranial pressure. It is doubtful whether papilledema ever develops subsequent to the appearance of primary atrophy of the optic nerve. Headache was outstanding at some stage in 10 of the 11 cases and vomiting was present in 5 cases.

DIAGNOSIS

This type of tumor occurs predominantly in children or young adults, but doubtless it may remain small and asymptomatic for many years. In 5 cases symptoms had appeared before the patient was 10 years old, but in most instances several years had elapsed before the patients presented themselves for treatment. The oldest patient was a man aged 52, who had had a progressive loss of vision for four years (case 9).

The result of neurologic examination was as a rule, essentially negative from an objective standpoint. In 4 cases there was definite mental disturbance, which consisted chiefly of lack of cooperation and failing memory. In case 11 the patient was so disturbed mentally that one physician had considered him psychotic. In 2 cases there was a clear history of recurrent olfactory hallucinations. The systolic blood pressure was uniformly low in each case.

Roentgenograms of the head disclosed positive evidence of bony erosion of the sella turcica in 10 of the 11 cases (fig 1), contrary to many reports, this was the most constant single positive finding. Suprasellar calcification of varying degree was evident in 8 of the 11 cases; this percentage of cases is similar to that usually reported by other authors.²³

23 Camp J D. Intracranial Calcification and Its Roentgenologic Significance, *Am J Roentgenol* **23** 615-624 (June) 1930. Cushing, H. The Intracranial Tumors of Preadolescence. *Am J Dis Child* **33** 551-584 (April) 1927. Drury, W E. Brain Tumors. General Diagnosis and Treatment in Lewis D. Practice of Surgery, Hagerstown Md. W F Prior Company, Inc., 1932 pp 443-674. Luger A. Zur Kenntnis der im Röntgenbild sichtbaren Hirntumoren mit besonderer Berücksichtigung der Hypophysengangsgeschwülste. *Fortschr a d Geb d Röntgenstrahlen* **21** 605-614 1914.

DIFFERENTIAL DIAGNOSIS

In the absence of definite suprasellar calcification, patients who have visual disturbances and erosion of the sella turcica, with or without evidence of increased intracranial pressure, may present a very difficult problem in preoperative diagnosis. Although the age of the patient and the symptom complex may strongly suggest the presence of a tumor of the hypophyseal duct, there are other lesions which may produce similar evidence of chiasmal or prechiasmal involvement.

Adenoma of the pituitary body produces a characteristic balloon-like enlargement of the sella turcica, bitemporal hemianopia and varying degrees of pituitary dysfunction. Meningioma generally occurs later in life than does tumor of the hypophyseal duct, it often is associated with local osseous proliferation and an increased local vascularity of the skull. Primary tumor of the optic nerves or optic chiasm²⁴ generally causes a more rapid visual loss, which is often associated with an enlargement of the optic foramina. A vascular lesion in the region of the chiasm, such as an aneurysm of the circle of Willis or of the internal carotid artery, may produce visual disturbances and local erosion of bone. Bizarre lesions of the midbrain must be considered, as well as local inflammatory reactions that produce chronic chiasmal arachnoiditis.²⁵ A tumor of the brain remote from the optic chiasm may at times closely simulate a primary involvement of this region. Obstructive hydrocephalus associated with dilatation of the third ventricle often produces chiasmal signs and secondary erosion of the sella turcica.²⁶

TREATMENT

Medical measures have no place in the treatment of a tumor of the hypophyseal duct. They afford only temporary symptomatic relief. Palliation results only in more serious loss of vision or in gradual increase in the intracranial pressure. This type of tumor, as Cushing¹⁰ has stated, presents the most difficult problem in neurosurgery.

Radical surgical removal of the tumor offers the patient his only ray of hope, but this procedure is rendered exceedingly difficult by the relatively inaccessible situation of the lesion. The growth is surrounded at its base by vital structures which cannot be sacrificed and which will tolerate little, if any traction or manipulation. Anteriorly are the optic nerves, laterally are the carotid arteries and posteriorly is the brain stem.

24 Love, J. G., and Kernohan, J. W. A Ganglioneuroma of the Optic Chiasm, *Proc. Staff Meet., Mayo Clin.* **12** 300-304 (May 12) 1937.

25 Craig, W. M., and Lilje, W. I. Chiasmal Syndrome Produced by Chronic Local Arachnoiditis. Report of Eight Cases, *Arch. Ophthalmol.* **5** 558-574 (April) 1931.

26 Bailey, P. Concerning the Cerebellar Symptoms Produced by Suprasellar Tumors, *Arch. Neurol. & Psychiat.* **11** 137-150 (Feb.) 1924.

The circle of Willis completely surrounds the base of the tumor and thus adds materially to the difficulty of the surgical treatment

As a rule the tumor has reached a considerable size by the time the patient presents himself for surgical treatment. Consequently, one is generally confronted with the problem of removal of a growth which has involved the third ventricle, has distorted and compressed the mid-brain and has become intricately entwined in the diffuse arterial network at the base of the brain. Simple aspiration of the cystic portion of the tumor will naturally relieve the pressure but such a procedure alone is of little value, as the cavity rapidly refills and the symptoms return. The most satisfactory surgical management consists in aspiration and collapse of the cyst followed by as nearly complete a removal of the capsule as is anatomically possible.

In the pioneer days of neurosurgery the transsphenoidal approach was the accepted method of dealing with a lesion in the region of the optic chiasm. Although this method allowed access to the sella turcica it was extremely unsatisfactory in an attempt to remove a lesion in which there had been suprasellar extension. In addition to the obvious anatomic limitations of this approach, there was always extreme risk of infection from the nasal cavity. Indeed death from postoperative meningitis was fairly common when this method was in vogue.

Within the past ten years the intracranial transfrontal operation has completely supplanted the transsphenoidal method. With the advent of this approach the operative mortality and ultimate results have evidenced a decided improvement.²⁷ There is no longer the constant threat of post-operative infection provided strict surgical asepsis is observed. The improved visualization of the entire anterior fossa of the cranium permits more accurate and extensive dissection and mobilization of the tumor.

The question of the side on which the transfrontal craniotomy is to be performed is generally decided on the basis of visual acuity. Experience has shown that the most satisfactory results are obtained in cases in which surgical removal is carried out on the side corresponding to the eye which shows the more marked visual loss. However in cases in which the diminution of vision is equal bilaterally the operation of choice is a transfrontal craniotomy on the right in view of the slighter post-operative reaction which follows manipulation of the right frontal lobe of the brain.

Craniotomy is performed through an anterior midline incision carried as far posterior as the coronal suture and then curved laterally to

²⁷ Adson, A. W. Operability of Brain Tumors. *Ann Surg* **100** 241-265 (Aug.) 1934. The Surgical Consideration of Brain Tumors. *Northwestern Univ. Bull. Med. School* **35** 1-42 (Dec. 31) 1934.

end in the posterior inferior temporal region (fig 5) The skin and bone flaps are reflected separately The anterior limb of the latter must be parallel to the supraorbital ridge and sufficiently far anterior to allow easy access to the floor of the anterior fossa The approach to the optic chiasm may be made on either side of the dura mater and under the frontal lobe of the brain The extradural method is preferable, but on occasion exposure may be improved by incising the dura over the frontal lobe and proceeding intradurally The extradural approach becomes intradural at the lesser wing of the sphenoid bone

In the presence of internal hydrocephalus, evacuation of the lateral ventricle by tapping of the anterior horn usually will afford adequate room beneath the frontal lobe by partially collapsing the hemisphere

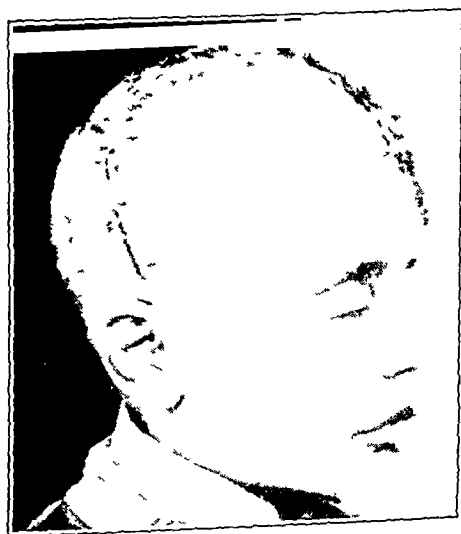


Fig 5—Postoperative photograph of a patient (case 7), showing the type of scalp incision employed in operation for a tumor in the region of the optic chiasm

Prior to the introduction of intratracheal anesthesia it often was necessary to administer a hypertonic solution of dextrose intravenously to shrink the hemisphere and facilitate exposure of a tumor in the chiasmal region In the absence of generalized increased intracranial pressure, adequate exposure is obtained relatively easily when intratracheal ether anesthesia is used

The intratracheal tube suggested by Magill provides an adequate and free airway This eliminates straining and difficult respiration which produces venous engorgement with resultant increase in the intracranial tension, which in turn makes adequate exposure impossible without exertion of extreme traction on the frontal lobe of the brain Aspiration of the cystic portion of the tumor is generally followed by collapse of the growth, which greatly reduces the tension within the

anterior fossa. In favorable cases collapse of the cystic portion affords sufficient exposure for gradual (piecemeal) removal of the tumor. Extreme care must be exercised at this point to avoid injury to the *circulus arteriosus* and the anterior cerebral arteries, which may be embedded in the tumor. It is inadvisable to attempt to remove the growth intact, as this is usually impossible without irreparable injury of the adjacent structures.

Careful, gentle handling of the tissues cannot be overemphasized in this as in all neurosurgical procedures. Well timed blood transfusions we feel are of inestimable value in such a case. Blood administered at the time the anterior fossa is being explored prior to removal of the tumor, appears to reduce greatly the degree of surgical shock as well as to supply the patient with some unknown factors which greatly aid his subsequent convalescence. The specific value of routine blood transfusion during the removal of such a tumor cannot, of course, be accurately estimated. Nevertheless experience has shown that there is definitely more than a casual relation, and it is believed that routine transfusion in these cases will be followed by improved surgical results. Seven of our patients received transfusion (indirect sodium citrate method) on the operating table, although the blood was not needed to combat shock. One patient was given transfusion the day after the operation because of persistently low blood pressure. The question of drainage of craniotomy wounds is subject to much debate. Without entering a long discussion we should like to say that it is our feeling that drainage of the wound for a period of twenty-four to forty-eight hours is of distinct value. Drainage was employed in every case in this series. Usually two Penrose cigaret drains are employed. One is placed under the frontal lobe, which has been elevated in order to facilitate removal of the tumor. This drain is extradural and does not come in contact with the optic nerves or the *cortex cerebri*. The other drain is left between the musculo-osseous flap and the scalp. The external ends of the drains are brought out through the posterior limb of the wound. Rarely, the first drain is brought straight out through a stab wound in the anterior temporal region.

In operations on children among whom tumor of the hypophyseal duct is most often seen the time factor is worthy of careful consideration. We hesitate to discuss this point because after all accurate diagnosis, extreme consciousness of aseptic precautions and carefully planned and executed surgical technic combined with well administered anesthesia are the principal determinants of a successful outcome. However craniotomy is a notoriously long procedure and if it can be shortened without sacrifice of accurate hemostasis and safety this will be a boon to the surgeon and probably contribute to a lowering of mortality.

During the past year and a half, in the hospital service of one of us (J. G. L.) it has been customary to close the muscle, the temporal fascia and the galea aponeurotica of the supratentorial craniotomy wounds in operations performed for benign lesions with continuous catgut sutures instead of interrupted sutures of silk as was previously done. This saves a great deal of time and, so far as can be determined, has not caused any untoward developments in the healing of the wounds.

The average time required for the performance of each of these 11 reported operations was three hours and five minutes. The longest operation required four hours and fifteen minutes, and the shortest, one hour and forty-five minutes.

Postoperative care of the patient, which should include timely lumbar punctures for drainage and administration of pituitary preparations in case of water imbalance, is very important, tending to reduce morbidity and possibly mortality.

After the removal of the Penrose cigaret drains (twenty-four to forty-eight hours after the operation), if the patient complains of headache or has fever or stiffness of the neck a lumbar puncture is performed while the patient is in the horizontal position on his side, with the craniotomy wound uppermost to avoid pressure and discomfort. The pressure of the cerebrospinal fluid is determined with an Ayer manometer, and the pressure is reduced slowly to half of the original value. If the fluid is bloody or xanthochromic, spinal punctures should be performed daily until the fluid is clear. Two or three punctures usually are sufficient.

If the water balance is negative, that is, if the urinary output is greater than the total fluid intake, posterior pituitary should be administered. Usually, 0.5 cc. of a solution of posterior pituitary administered hypodermically twice daily will correct the fluid discrepancy and relieve the thirst which is a usual accompaniment. A few days of this therapy will usually suffice. If the imbalance should recur, nasal insufflation of powdered posterior pituitary is a better method of treatment. The patient can administer this preparation in this manner without aid and without a hypodermic syringe.

REPORT OF CASES

CASE 1—A girl aged 5 years was brought to the clinic April 15, 1935, because of progressive impairment of vision. She had been well until one year prior to her registration, when the parents noted that her vision was not normal and that her right eye turned outward. She never had headache or nausea, and she had not vomited. The values for the systolic and diastolic blood pressure were 88 and 58 mm. of mercury, respectively, and the pulse rate was 92. The results of general examination were essentially negative.

Ophthalmologic examination revealed only light perception in the right eye and the ability to count fingers at 10 feet (3 meters) with the left eye. There

was temporal hemianopia in the left eye, and there was only a residual temporal field in the right eye. Fundusoscopic examination disclosed evidence of bilateral atrophy of the optic nerve. There was convergent strabismus of the right eye. The pupils and reflexes were normal.

Roentgenograms of the head revealed a calcified tumor 5 cm in diameter just above and anterior to the sella turcica. Calcification had occurred in the walls of the tumor. There was evidence of secondary erosion of the sella turcica and thinning of the floor of the anterior fossa on the left side. Neurologic examination disclosed no abnormality. A diagnosis of suprasellar cyst was made. A transfrontal craniotomy on the right side was performed intratracheal ether anesthesia being used. The anterior horn of the right lateral ventricle was tapped, this allowed the brain to collapse and permitted excellent exposure. A very large cystic tumor was found; its position was both intrasellar and extrasellar. Both optic nerves were displaced laterally and were stretched to several times their normal length. Aspiration of 4 ounces (120 cc) of thick dark yellow fluid collapsed the cyst, which was then incised and a large amount of grumous material was removed. The cyst was removed and the third ventricle was opened. The wound was closed in the usual anatomic manner. One Penrose drain was left adjacent to the sella turcica and one was left between the scalp and the bone flap. The microscopic diagnosis was tumor of the hypophyseal duct. Convalescence was entirely uneventful. The patient was dismissed on the fifteenth postoperative day. The results of another neurologic examination which was made before the patient was dismissed were essentially negative. It was observed that the strabismus had entirely disappeared. Visual acuity at the time of the patient's dismissal was approximately the same as at the time of the original examination.

Comment—This case illustrates the tragic result of postponing surgical intervention when pressure on the optic nerves has developed. It further emphasizes the irreparable atrophy of the optic nerve which results from long-continued local pressure.

CASE 2—A man aged 26 was referred to the clinic in July 1935 because of headaches and an endocrine disturbance. He said that he was well until the age of 9 years; however, at the age of 6 or 7 years he had severe headaches which occurred periodically for two years. He stopped growing at the age of 9 years. He did well in school until his junior year in high school, when he failed in several courses and found it difficult to concentrate. His voice did not change. Between the ages of 21 and 26 his height increased 4 inches (10 cm). Two years prior to his admission to the clinic he noted decreased vision in the left eye, decrease progressed gradually. The nasal field in the left eye was the last to lose its vision and for a year before the patient came to the clinic he was completely blind in the left eye. A short time before he came to the clinic he noted that he bumped into objects to his right unless he turned his head. Periodic peculiar odors and visual hallucinations associated with olfactory hallucinations were noticed three or four times a week during the year prior to his admission. Generally he felt well except for tiredness and drowsiness which had been noted a short time before he came to the clinic.

The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 84 and 62 mm of mercury respectively and the pulse rate was 72. The patient's features were those of a boy of 11 or 12. Endocrine dysfunction was evidenced by the absence of body hair and by the narrow shoulders, broad hips, pads of fat over the pubes and trochanters, short trunk, long slender arms and long tapering fingers.

The face was smooth and beardless. The skin appeared soft, white and smooth. The voice was high pitched. The prostate gland was rudimentary, and the genitalia were infantile. Ophthalmologic examination disclosed amaurosis in the left eye and 6/5 vision in the right eye. There was temporal hemianopia in the right eye, and marked primary atrophy of the optic nerve was present in the left eye. Roentgenograms of the head revealed enlargement, grade 3, of the sella turcica and destruction of its floor. The posterior clinoid processes and the dorsum sellae were eroded. Neurologic examination revealed moderate generalized weakness of the arms and legs. The deep tendon reflexes were diminished or absent, even on reinforcement. The Babinski phenomenon was present on the right side. The direct light reflex was absent in the left eye. The diagnosis was tumor of the pituitary body.

With the patient under intratracheal ether anesthesia, a transfrontal craniotomy was performed on the left. The brain was tense, and the dura bled freely. An attempt to tap the left anterior horn was unsuccessful. Careful elevation of the left frontal lobe disclosed a large cystic tumor which filled the sella turcica and displaced the optic chiasm posteriorly. The left optic nerve was flattened, and only a small part of its substance remained. The right optic nerve was less involved but was much smaller than usual and appeared concave on the mesial aspect as a result of local pressure. The capsule of the tumor was opened, and a large amount of dark brown grumous material, which contained crystals of cholesterol, escaped. Very little solid tissue was present in the tumor. A subtotal removal of the capsule was easily effected without trauma to the adjacent structures. A Penrose cigaret drain was placed beneath the frontal lobe, and another was placed between the skin and the bone flap.

The convalescence was uneventful. Another neurologic examination, made before the patient left the clinic, revealed essentially the same findings as were obtained before operation, this was also true of examination of the ocular fundi and visual fields, except that light perception was present in the left eye and subjective visual improvement was noted in the right eye. The pathologist made a diagnosis of tumor of the hypophyseal duct.

CASE 3—A man aged 31 was admitted to the clinic on Dec 12, 1935, because of progressive impairment of vision. He always had been nervous, shy and slightly backward. He stuttered until he was of high school age. Six months before his registration at the clinic he had "the flu," which lasted about one week. Soon thereafter he first noted that the vision in the right eye was not normal. Photophobia and further impairment of sight developed, as well as a "blind spot" in the right eye. Dull frontal headaches began about this time. They occurred two or three times a week and were worse in the evening. There were also periodic sharp pains in the frontal region. The headache was intensified by stooping, jarring and straining. Three months before he came to the clinic vomiting occurred, associated with nausea. The vomiting occurred intermittently and was worse when he became nervous or when he suddenly assumed an erect posture.

The patient was pale. The values for the systolic and diastolic blood pressure were 110 and 82 mm of mercury, respectively, and the pulse rate was 74. There was a feminine distribution of pubic hair. Ophthalmologic examination revealed visual acuity to be 6/10 in the left eye, and the patient was able to count fingers with the right eye. Examination of the visual fields revealed bitemporal hemianopia (relative), a central scotoma in the right eye and enlarged blind spots in both eyes. Funduscopic examination disclosed a suggestive pallor in the left eye and in the temporal portion of the right optic disk. The diagnosis was

chiasmal lesion, more prechiasmal on the right than on the left. Roentgenograms of the head disclosed enlargement grade 3, of the sella turcica, there also was evidence of erosion of the floor of the sella turcica and of the posterior clinoid processes. There was slight calcification at the outlet of the sella turcica. The diagnosis was chiasmal lesion.

With the patient under intratracheal ether anesthesia, a transfrontal craniotomy was performed on the right. The right optic nerve was swollen and had been displaced mesially and upward by a reddish purple mass which was situated between the nerve and the right ophthalmic artery, which was displaced laterally. The left optic nerve appeared normal. The tumor appeared to have arisen from within the sella turcica, but it extended beyond the confines of that structure. The cystic mass was aspirated, and yellow fluid was obtained. The capsule was split, and a large quantity of gray grumous material was aspirated through a brain cannula. A portion of the capsule was resected. Cholesterol crystals were clearly visible floating on the physiologic solution of sodium chloride while the anterior fossa was being irrigated. The wound was closed in the usual anatomic manner, one Penrose cigaret drain was left in the anterior fossa. Convalescence was uneventful. The patient was dismissed from the hospital on the twelfth postoperative day. Microscopic examination revealed a typical tumor of the hypophyseal duct. A neurologic examination made before the patient left the clinic did not reveal any abnormality. Ophthalmologic examination disclosed improvement in vision which was 6/7 in the left eye and 6/12 in the right eye. The pallor of the optic disk remained the same as prior to operation. Examination of the visual fields revealed a questionable homonymous defect on the left, which had become much fuller in extent.

CASE 4—A boy aged 5 years was brought to the clinic on April 27, 1936, because of headaches, vomiting and diplopia. About four months prior to his registration the patient began to complain of headaches which usually were worse in the morning. At the time he was brought to the clinic they had become more frequent and more severe. About three weeks prior to his examination it was noticed that his left eye turned in. At times he became very drowsy. This drowsiness would persist for several days and then disappear. There was constipation for two or three months prior to his admission to the clinic. The values for the systolic and diastolic blood pressure were 82 mm and 60 mm or mercury, respectively. The pulse rate was 76 and the temperature was 99.6 F. A definite cracked pot note was elicited by percussion of the head. Ophthalmologic examination disclosed papilledema of 4 diopters on the right side and 3 diopters on the left side. There were no hemorrhages. On account of the age of the patient and the lack of cooperation the visual fields were not determined. Roentgenograms of the head revealed increased intracranial pressure, enlargement of the sella turcica, erosion of its floor and of the posterior clinoid processes and small areas of calcification within and just above the sella turcica. Neurologic examination did not disclose any abnormality. The diagnosis was cyst of Rathke's pouch.

On May 2, 1937, with the patient under ether anesthesia, a transfrontal craniotomy was performed on the right. The contents of a suprasellar and intrasellar cyst were removed and the wall of the cyst was resected. Because of increased intracranial pressure it was necessary to tap the anterior horn of the right lateral ventricle and evacuate a large quantity of cerebrospinal fluid before the right frontal lobe could be elevated sufficiently to permit exploration of the region of the sella turcica. When the frontal lobe had been elevated and

the dura mater incised along the wing of the sphenoid bone, the right optic nerve was easily exposed. To the left of this nerve there was a large, blue thin-walled cyst. The wall of the cyst contained calcium. The cyst was opened, and 20 cc of greenish yellow fluid which contained cholesterol crystals and a large quantity of calcium was obtained. When the cyst had been collapsed, the anatomic structures about the sella turcica were identified, and it was noted that the bulk of the cyst was situated on the left of the left optic nerve, the optic chiasm and the left internal carotid artery. The optic chiasm was ballooned out and appeared cystic. The chiasm was not incised, as it was felt that the apparent cystic change in this structure might well be the result of edema secondary to stasis caused by local pressure by the tumor. The wall of the tumor was gradually coagulated by means of the electrosurgical unit and was partially resected. When the tumor had been removed, the optic nerves and optic chiasm appeared to have been decompressed completely. A Penrose cigaret drain was left under the right frontal lobe and brought out through the posterior limb of the craniotomy incision. The patient's convalescence was satisfactory, and the wound healed by primary intention. Microscopic examination of the tissue removed at operation revealed the characteristic appearance of a tumor of the hypophysial duct. Postoperative neurologic examination did not reveal any change in the preoperative condition, ophthalmologic examination disclosed receding papilledema and some secondary atrophy of the left optic nerve.

This patient recently underwent another craniotomy elsewhere, because of a recurrence of the symptoms.

CASE 5—A youth aged 18 registered at the clinic on Oct 9, 1936, because of headaches, vomiting and impairment of memory. The first attack of headache occurred in 1931. This attack was associated with vomiting, which lasted six to eight hours. The attack was followed by exhaustion. The second attack occurred in 1932, this was followed by similar ones in 1933 and 1934. Each succeeding attack was more severe and lasted longer than the previous one. The patient said that his general health between attacks was good. In 1935 his lack of physical development was noted, and a diagnosis of dystrophia adiposogenitalis was made. He was given thyroid extract, and later high voltage roentgen therapy was applied to the sellar region. After the roentgen therapy he became very ill for three weeks, severe headache, vomiting and malaise were present. Two months before he came to the clinic, administration of solution of posterior pituitary produced marked improvement. He did not vomit while this preparation was being administered. However, the headache was not relieved. During the few months prior to his admission to the clinic the patient became more drowsy, his memory became very poor, and vomiting not only reappeared but became projectile. The patient was underdeveloped for his age, he had the stature of a child of 12 years. He had a feminine type of deposition of fat and lacked secondary sexual characteristics. The values for the systolic and diastolic blood pressure were 94 and 66 mm of mercury, respectively. The pulse rate was 68. There was a wax pallor, the skin was dry but soft. A bruit was heard in both temporal areas. Ophthalmologic examination disclosed 6/10 vision in the right eye and the ability to see moving objects with the left eye. Examination of the visual fields revealed bitemporal hemianopia (residual nasal field). Examination of the ocular fundi disclosed moderate temporal pallor of the right optic disk and generalized pallor, grade 3, of the left optic disk. Roentgenograms of the head revealed diffuse calcification in the midline at the outlet of the sella turcica and some destruction of the dorsum sellae (fig 1). The diagnosis was tumor of the hypophysial duct.

On Oct 20, 1936, with the patient under ether anesthesia, a transfrontal craniotomy was performed on the left. The ether was administered through an intratracheal tube. The frontal lobe was tense and the brain was elevated with considerable difficulty. Numerous adhesions were present between the brain and the underlying tumor. A characteristic thin-walled cyst which contained calcium was found. Aspiration of the cyst produced approximately 20 cc of brownish fluid, which contained crystals of cholesterol. The portion of the cystic wall which could be easily mobilized after collapse of the cyst was carefully resected. There had been compression of the optic nerves and, although the greatest visual loss was on the left side the left optic nerve appeared larger and more nearly normal than the right. The wound was closed in the usual anatomic manner, two Penrose cigaret drains were inserted as a precautionary measure. The microscopic diagnosis was tumor of the hypophyseal duct. The wound healed by primary intention, and the convalescence was uneventful except for a period between the third and the sixth postoperative days, when spinal puncture was done on two occasions to relieve a moderate degree of increased intracranial pressure. The convalescence thereafter was satisfactory. The patient was dismissed from the hospital on the twelfth postoperative day, at which time his condition was

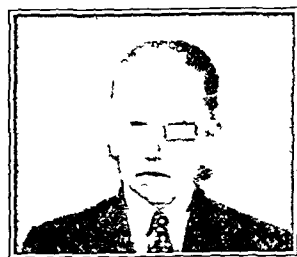


Fig 6—Postoperative photograph of the patient in case 5, the picture was taken two weeks after the operation

excellent and his vision much improved (fig 6). He was able to recognize gross objects with his left eye. A recent report stated that his general health was excellent, that his vision was very good that he could read well with either eye and that he had had no headaches since he left the clinic.

CASE 6—A man aged 33 registered at the clinic May 25, 1936 because of headaches which had occurred for one year. He had had frontal headaches as far back as he could remember, but these had not been as severe as the headaches which occurred during the year before he came to the clinic. The latter were bilateral frontal headaches, at times the pain extended to the occipital region. The headaches occurred daily and were of increasing severity. For about one month prior to registration the attacks were periodic and characterized by an aura. During these attacks he felt as if he were going to lose consciousness. The attacks were followed by a peculiar odor which smelled like medicine. These uncinate attacks lasted about a minute and were followed by an increase of pain in the head. They occasionally awakened him at night. He often had as many as three or four attacks during the day, and at times he had to leave his work and lie down. The patient felt that his memory for recent events was failing. Because of blurring of vision he consulted his local physician who prescribed glasses. These produced temporary relief. There was a loss of the sense of

The results of general physical examination were essentially normal. The values for the systolic and diastolic blood pressure were 111 and 72 mm. Hg respectively. The pulse rate was 72. Ophthalmic examination disclosed a visual acuity of 6/6 in the right eye and 6/5 in the left eye. Examination of the fundi disclosed blurring about the nasal margins of both optic disks without any serious correction. The arteries and veins were dilated, this suggesting a local effect of the optic disk. However, there was no measurable elevation of the optic disk. Perimetry disclosed complete right homonymous hemianopia. The roentgenograms of the head disclosed an irregularly calcified shadow, which was situated within and extended above the sella turcica. There also was evidence of secondary erosion of the floor of the sella turcica, of the posterior clinoid processes and of the dorsum sellae.

On June 1 a transfrontal craniotomy was performed on the right. The brain was under definitely increased pressure, and it was with difficulty that the right frontal lobe was elevated sufficiently to expose the large thin-walled cystic tumor

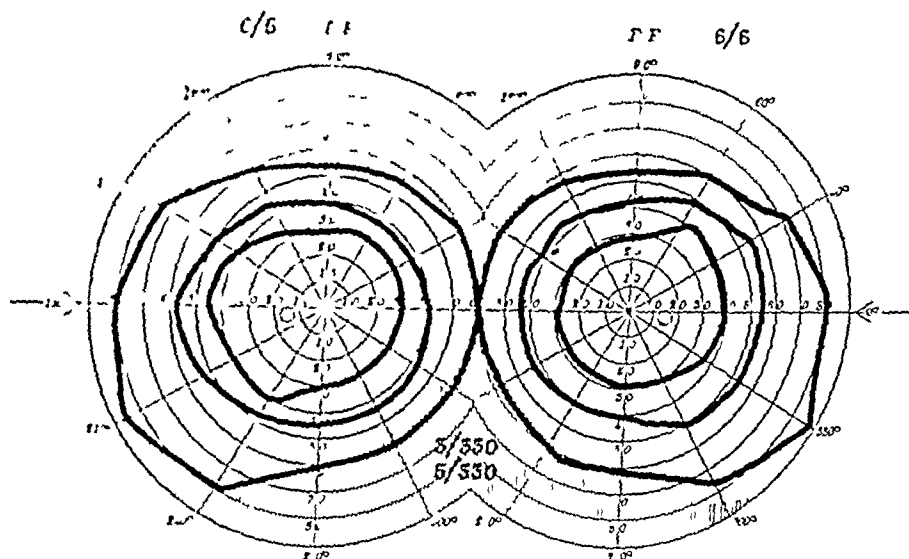


Fig 7—Normal fields of vision with normal central vision after removal of a tumor of the hypophyseal duct (case 6)

which was situated to the left of the optic chiasm and the left optic nerve and which had displaced these structures to the right. The thin wall of the cyst contained a large quantity of calcium. Three ounces (90 cc.) of yellow fluid, which was loaded with cholesterol crystals, was obtained from the tumor. Aspiration collapsed the wall of the cyst and reduced the intracranial pressure sufficiently to permit excellent exposure of the structures about the sella turcica. The right optic nerve was about normal in length and was only slightly displaced. The left optic nerve, however, was definitely elongated and arched toward the right side. The capsule of the tumor was delivered beneath and around the left optic nerve and removed. A Penrose cigaret drain was left under the right frontal lobe and was brought out through the posterior limb of the craniotomy wound. Histologic examination disclosed a typical tumor of the hypophyseal duct. The wound healed by primary intention, and the patient's convalescence was rapid. He was dismissed from our care on June 16, at this time he was free from headaches, and neurologic examination did not disclose any abnormality except the loss of the sense of smell.

There had been no recurrence of the uncinate attacks. Vision was normal, and the visual fields were normal (fig 7). There was no edema of the optic disks.

CASE 7—A boy aged 11 was brought to the clinic on Aug 8, 1936, because of progressive loss of vision in both eyes. Three years prior to his admission, during a routine physical examination at school, a nurse noted defective vision in his right eye. The child however, did not complain of poor vision until one year before he came to the clinic. One month before his admission, frontal headaches occurred daily for three weeks. They were moderately severe. From the time he was 18 months of age his nose bled frequently; the epistaxis was always worse in hot weather. During the month before his admission epistaxis occurred daily and often was preceded by headache, which was relieved after his nose had bled for a few minutes. The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 96 and 62 mm of mercury respectively. The pulse rate was 78.

Ophthalmic examination revealed that vision was 6/10 in the left eye and 6/30 in the right eye. Relative bitemporal hemianopia and relative central scotoma of the right eye were disclosed. The optic disks appeared taut nasally but were not definitely edematous. There was pallor grade 1 of the temporal part of the right optic disk, but there was no definite pallor of the left optic disk. Roentgenograms of the head revealed enlargement of the sella turcica and slight thinning of its floor and of the posterior clinoid processes. Neurologic examination did not reveal any abnormality. There was no evidence of endocrine dysfunction, although the child was puny, pale and listless. The diagnosis was chiasmal lesion.

A transfrontal craniotomy was performed on the right, with the patient under intratracheal ether anesthesia. A large suprasellar and intrasellar thin-walled cyst was found, this was situated in front of the optic chiasm and had displaced both optic nerves laterally. Approximately 25 cc of thick yellow fluid was removed, and a considerable proportion of the wall of the cyst was removed. The cyst contained a great deal of calcium. A portion of the capsule of the cyst, which was behind and under the optic chiasm, could not be removed but both optic nerves were thoroughly decompressed. One Penrose cigaret drain and one Penrose drain were inserted, and the wound was closed in the usual anatomic manner. Convalescence was satisfactory, and the wound healed by primary intention (fig 5). Histologic examination revealed a typical tumor of the hypophyseal duct. Post-operative neurologic examination did not reveal any abnormality. Ophthalmic examination demonstrated great improvement in the vision. The vision in the left eye was 6/6, and that in the right eye was 6/30. No significant change had occurred in the ocular fundi since the previous examination. The visual fields showed marked improvement, that of the left eye was reported as normal and there was only a suggestive temporal notch in the visual field of the right eye. However, the relative central scotoma remained unchanged. When the patient was last heard from his condition was satisfactory and there had been no further loss of vision.

CASE 8—A woman aged 25 came to the clinic on Nov 25 1936, because of headaches and amenorrhea. Until the age of 17 she menstruated regularly at which time the menstrual periods began to be irregular. Amenorrhea for as long as three months occurred often. The menses gradually decreased in frequency and amount and from the age of 20 on amenorrhea prevailed. Many types of glandular therapy were tried without avail. For several years prior to her admission to the clinic she had headaches which became more severe during the last six months. No visual trouble had been noted by the patient. For the past

few months drowsiness had been marked. The drowsiness was increasing. The patient fell asleep easily and frequently. Although her mentality had become slower than usual, she was able to continue her work as clerk in a store. Two days before she came to the clinic she had the first attack of vomiting, which began at 4 a. m. "Convulsions" occurred four times during the following day, and one 'generalized' grand mal seizure was described by the home physician. Drowsiness increased. The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 108 mm and 75 mm of mercury, respectively. The pulse rate was 58. Ophthalmic examination disclosed normal visual acuity. Examination of the visual fields disclosed homonymous hemianopia of the right lower quadrant. Funduscopic examination revealed edema of the nasal margins of both optic disks. The elevation was 1 to 2 diopters in the right eye and 2 diopters in the left eye. Hyperemia of both optic disks and venous engorgement also were present. There were several hemorrhages along the veins in the right eye at some distance from the optic disk. Several small punctate hemorrhages were present near the macula, and there also were some large, deep hemorrhages in the same region. Roentgenograms of the skull revealed diffuse particles of calcification, which extended backward and upward from the dorsum sellae, and destruction of the superior portion of the dorsum sellae. Neurologic examination revealed that the attention, cooperation and memory of the patient were much below normal. The patient was obese. She was unsteady on her feet and seemed to totter to the left. She had difficulty when she tried to stand on her right or left foot while her eyes were closed, this difficulty was more marked when she attempted to stand on her left foot. The diagnosis was tumor of the hypophyseal duct.

In view of the right homonymous hemianopia, a left transfrontal craniotomy was performed on November 28, with the patient under intratracheal ether anesthesia. In spite of the choked disk the brain was not under great tension, and there was considerable fluid in the cisterna chiasmatica, which when removed allowed a satisfactory visualization of the optic chiasm. No tumor, however, could be seen. Elevation of the frontal lobes from the optic chiasm revealed a bluish tumor which was situated posterior to the chiasm, between the optic tracts. It was cystic and contained calcium in its walls. One ounce (30 cc) of brownish fluid was aspirated, which allowed the cyst to collapse. Extensive resection of the capsule of the tumor was then effected, which thoroughly decompressed the optic tracts and chiasm. Two Penrose cigaret drains were inserted. Histologic examination revealed a typical tumor of the hypophyseal duct.

Convalescence was stormy for the first few days, and there was weakness of the right arm and leg. There was gradual improvement in motor power. An acute elevation of temperature occurred on the sixth postoperative day but subsided immediately after aspiration of the flap and removal of several cubic centimeters of serum. At the time the patient was dismissed, on the twenty-second day, her condition was much improved. Neurologic examination did not reveal any abnormality except slight weakness on the right side, which was gradually improving. The vision was 6/6 in both eyes. The visual field appeared much improved, and the papilledema had entirely receded. When the patient was last heard from she was in good health, her appetite was excellent, and the weakness of the right side had decreased so that she was able to walk without a limp.

Comment—This case illustrates the great diversity of symptoms associated with this type of tumor. Although menstrual irregularity was present for years, no other definite symptoms appeared until six months

before the patient came to the clinic. She had never noted any visual difficulty, although bilateral papilledema was present and there was definite homonymous hemianopia of the lower right quadrants. The optic fundi presented an appearance not usually associated with increased intracranial pressure but it closely simulated that of retinitis septica such as is commonly seen in cases of subacute bacterial endocarditis. Repeated cultures of the blood were sterile. The site of the tumor was rather unusual, it was posterior to the optic chiasm and was situated between the optic tracts.

CASE 9—A man aged 52 registered at the clinic Jan. 11, 1937, complaining of progressive loss of vision.

Four years before the patient came to the clinic he discovered a loss of vision in the temporal half of the left eye. New glasses did not produce much relief. Six months later he noted that vision in the temporal field of the right eye was failing, and thereafter there was gradual but steady loss of vision except for one short period early in his illness when the vision first in the left and then in the right eye seemed to improve definitely for a few weeks. During the six months prior to his registration at the clinic the patient noticed diplopia for close objects. The second image appeared just above the real image. Headaches were present for three years, they were dull and throbbing and were situated in the left occipital and cervical regions. They were periodic and lasted only one to six hours beginning and ending abruptly.

The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 110 and 76 mm. of mercury, respectively. The pulse rate was 84. Ophthalmic examination revealed that the vision in the left eye was 6/30, a bitemporal visual defect and a central scotoma were present in the left eye. Examination of the ocular fundi revealed pallor, grade 2, of the right optic disk; there was no visible loss of substance. There was pallor, grade 3, of the left optic disk; there also was a loss of substance in the temporal portion of the left disk. Urinalysis disclosed no abnormality. The concentration of hemoglobin was 15.4 mg. per hundred cubic centimeters of blood. There were 4,500,000 erythrocytes and 7,500 leukocytes in each cubic millimeter of blood. The flocculation test for syphilis gave negative results. Roentgenograms of the head did not disclose any abnormality. Roentgenograms of the optic canal revealed that the right optic foramen was larger than the left; this probably was the result of an anatomic variation. Neurologic examination revealed no abnormality, the cerebrospinal fluid was normal. A diagnosis of chiasmal lesion was made.

A left transfrontal craniotomy was performed with the patient under intra-tracheal ether anesthesia. A large thin-walled cystic tumor was situated anterior to the optic chiasm. There were extensive adhesions between the tumor and both optic nerves. The cyst was aspirated and 20 cc. of dark dirty greenish material was removed. The capsule of the cyst was resected. A considerable amount of grumous material and flecks which resembled cholesterol crystals were found chiefly in the portion beneath the left optic nerve. Both optic nerves and the optic chiasm were thoroughly decompressed. The optic nerves appeared definitely smaller and paler than normal. Two Penrose cigaret drains were inserted and the wound was closed in the usual anatomic manner. Microscopic examination revealed a typical tumor of the hypophyseal duct. The convalescence was uneventful except for a few episodes of acute hypopituitarism which were

evidenced by low blood pressure and increased urinary output. These symptoms were controlled by hypodermic injections of a solution of posterior pituitary, they later were controlled by nasal insufflation of posterior pituitary. The patient was dismissed from the hospital two weeks after the operation. At that time the neurologic examination did not reveal any abnormality. The vision, which had improved, was reported as 6/7 in the right eye. Considerable improvement was also noted in the visual field. Only light perception was present in the left eye. The pallor of the optic disk was essentially the same as it had been at the time of the preoperative examination. When last heard from, the patient said that he had noticed much visual improvement. It has been necessary for him to continue endocrine therapy because of mild hypopituitarism.

Comment—In spite of the rather large lesion about the optic chiasm, there was no roentgenographic evidence of osseous change in the sella turcica. Definite evidence of osseous erosion is usually evident roentgenographically four or more years after the onset of symptoms, but for some unknown reason such evidence was not observed in this case.

The advanced age of the patient is unusual. This case illustrates the fact that a tumor anlage may lie dormant for many years and then, for some unexplainable reason, undergo cellular proliferation and form a tumor.

CASE 10—A girl aged 9 was brought to the clinic by her parents on Feb 8, 1937, because of headaches, vomiting and an almost total loss of vision. For five or six years prior to this she had afebrile attacks of vomiting, these attacks were preceded by nausea. They occurred every four to six weeks and lasted one or two days. The attacks continued, but there was no progression in their severity. One year before the patient was brought to the clinic, it was observed that her vision was much impaired. The patient's mother also noted that the right eye frequently turned upward and outward. The patient complained frequently of double vision. Four months before she came to the clinic she began to have frontal headaches. Just prior to her registration drowsiness and somnolence were noted by the parents for the first time. General physical examination revealed a systolic blood pressure of 90 mm of mercury and a diastolic pressure of 60 mm of mercury. A cracked pot sound could be elicited over the left frontal and parietal regions of the skull. Ophthalmic examination revealed that vision was 6/30 in the left eye and that the patient could perceive only light with the right eye. Examination of the visual field disclosed temporal hemianopia and a depressed field in the left eye and a residual nasal field in the right eye. Fundusoscopic examination revealed evidence of atrophy of the optic nerve, which was more advanced in the right eye than in the left. Roentgenograms of the head disclosed evidence of increased intracranial pressure, extensive destruction of the sella turcica and erosion of the anterior and posterior clinoid processes. Neurologic examination disclosed no abnormality. The diagnosis was tumor of the hypophyseal duct. Exploration was advised but not urged, in view of the grave surgical risk. The parents requested that operation be attempted in the hope of affording the child some degree of relief.

A transfrontal craniotomy was performed on the right with the patient under intratracheal ether anesthesia. A large, thick-walled cyst was exposed, it was situated between the optic nerves and had displaced the optic chiasm posteriorly. Thirty cubic centimeters of dark brown fluid was obtained by aspiration of the

cavity. The wall of the cyst was incised and a large amount of thick coarse material, which contained calcium was removed. Extensive resection of the capsule was carried out. The capsule was 1 cm thick in the more posterior portion, which was situated beneath the optic chiasm; however further anteriorly it became very thin, in certain portions measuring less than 1 mm in thickness. The optic nerves were unusually vascular. Two Penrose cigaret drains were inserted as a precautionary measure. The convalescence was uneventful. The results of another neurologic examination were essentially the same as those observed at the preoperative examination. There was subjective visual improvement in spite of the lack of objective evidence of improvement. The visual acuity was 4/6 in the left eye; only perception of light was present in the right eye. The patient returned to the clinic in four months because of attacks of excessive vomiting, which had occurred five or six times daily. Neurologic examination again failed to disclose any abnormality. Ophthalmic examination revealed a further reduction in vision.

CASE 11—A boy aged 16 was brought to the clinic on Jan 12, 1938 because of a distinct mental change. His illness began in the summer of 1937 when he had headaches in the frontal regions and over the vertex. In the fall of that year he complained of blurring of vision and diplopia when he was reading. At about the same time his grades, which formerly had been good, became very poor, and he failed to participate in the usual activities at school. On Jan 8, 1938, he became very drowsy; he fell asleep at the table and slept all day and all night. He lost all interest in things about him and his mental reactions were silly. He became facetious. His judgment became poor and there was a complete change in his personality. He walked up to strangers and pulled their ties and pulled their pencils out of their pockets; he also did many acts with compulsion. His appetite became enormous, and he gained considerable weight. Likewise there was an increase in thirst, with an increase in urinary output. His parents said that he drank a gallon of liquid a day and passed a corresponding quantity of urine.

His height was 5 feet 6½ inches (171.9 cm) and his weight was 144 pounds (65.3 Kg). The value for the systolic blood pressure was 100 mm of mercury, and that for the diastolic pressure was 60 mm. The pulse rate was 48. During the examination the patient was noisy. He giggled and shouted without cause. Ophthalmic examination revealed that vision was 6/30 in the right eye and 3/60 in the left eye. The examination disclosed pallor, grade 2, of the right optic disk and pallor, grade 1, of the left optic disk. There were small areas of pigment degeneration in each macula. Examination of the visual field revealed a right homonymous hemianopia of an incongruous type. There was a central scotoma in the left eye. The neurologic examination did not disclose any abnormality. Roentgenograms of the head revealed an irregular mass of calcium 2.5 by 3 cm, directly above the posterior clinoid processes. The tumor appeared to be in the midline and there was some evidence of pressure erosion of the left posterior clinoid process. The roentgenographic evidence suggested that the tumor probably involved the third ventricle. An encephalogram disclosed evidence of a suprasellar tumor which occupied a position corresponding to the position of the calcium seen in the original roentgenograms. The third ventricle was displaced upward and backward by the tumor mass. In view of these findings the diagnosis was tumor of the hypophyseal duct.

On January 20 a transfrontal craniotomy was performed on the left. This disclosed a large thin-walled cystic tumor which was situated posterior to the optic chiasm. This made adequate exposure of the tumor difficult. The only

approach to the tumor was behind the optic chiasm and anterior to the anterior communicating artery. A hollow needle was inserted through the thin wall of the tumor and about 20 cc of yellow fluid was removed. This collapsed the cystic tumor and removed the abnormal pressure from the optic tracts and optic chiasm. Only a small portion of the capsule was resected, because of the inaccessible position of the tumor. Microscopic examination of the capsule of the tumor revealed a typical tumor of the hypophyseal duct. The wound was closed in the usual manner after one Penrose cigaret drain had been inserted beneath the left frontal lobe and another between the scalp and bone flaps. During the operation a transfusion of 500 cc of citrated blood was given. The patient's convalescence was characterized by intermittent fever. His temperature ranged from normal to 102 F daily. However, his general condition seemed to be excellent, and he was mentally clear and alert. Another neurologic examination disclosed the same mental reactions as had been present prior to the operation. Postoperative ophthalmic examination revealed no change except a mild edema of the nasal portion of the left optic disk.

SUMMARY

Tumor of the hypophyseal duct is extremely rare. Few articles on the subject have been published. It is hoped that the present report of a series of 11 consecutive cases in which operation was performed without a death will stimulate other physicians to take a more active interest in this condition and to make the diagnosis early, before irreparable injury has been caused by long-continued pressure on the visual pathways.

Although the presenting symptoms are usually those referable to the eyes, glasses and medical treatment are not beneficial in counteracting the pressure effects of an intracranial neoplasm. Transfrontal craniotomy with as extensive removal of the tumor as is consistent with good surgical judgment is the treatment of choice.

Organotherapy is useful and is indicated in some cases, but its role is secondary to that of removal of the tumor.

CONCEALED CHRONIC ALCOHOLISM IN SURGICAL PATIENTS

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It seems worth while to present some facts about surgical patients who may be said to be suffering from a condition I wish to call concealed chronic alcoholism. The obvious case of addiction to alcohol can hardly be excluded from the study until the diagnosis is actually made by the surgeon treating the patient. Then the diagnosis chronic alcoholism is added to the surgical diagnosis.

The need of recognition of all types of alcoholism in patients with surgical conditions is emphasized and illustrated in certain cases which I have observed and which I shall describe. In this report the term concealed chronic alcoholism is used for the first time so far as I know. If there is a condition deserving the name concealed chronic alcoholism, there are, I believe, means of making the diagnosis. Some of these are herein detailed.

Acute alcoholism is as a rule comparatively easy to recognize except when such severe conditions as coma have supervened. In many cases of glandular imbalance, organic disease and trauma the odor of alcohol on the breath may mislead the examiner. The further examples of tumor or abscess of the frontal lobe, insulin shock, diabetic ketosis, uremia and various injuries of the skull need only to be mentioned to remind one that a complete analysis of every case is necessary to avoid attributing to alcoholism the symptoms of some other condition.

A patient who is a victim of true chronic alcoholism may show no clearcut signs if the taking of the history, the physical examination and the laboratory analysis are carried out in a cursory manner. A list of all the findings in a questionable case, however, should furnish clues by which to reach the diagnosis of acute or chronic alcoholism or concealed chronic alcoholism.

The most common symptoms of true alcoholism are the following: tremors of the eyelids, tongue, the facial muscles, hands and even legs; erythema or flushing of the face or sometimes pallor; acne-like cutaneous eruption of the face, telangiectases of the face, atrophy of the limbs; obesity or emaciation; poor muscular coordination; evidence of peripheral neuritis; disorientation; hypoaesthesia; paresthesias; rattly heart.

hypertension, albuminuria, venous engorgements, especially of the head, headache, mental depression; dizziness and vertigo, irritability and restlessness, insomnia, polyuria, tachycardia, tinnitus, dyspnea, palpitation, precordial pain, physical and mental weakness, moral deterioration, delirium tremens, gastric upsets, colitis, constipation and variable appetite for certain foods, dysphagia, hoarseness, and even purpura and cirrhosis of the liver.¹ Some of the pigment changes seen in the skin of drunkards are unquestionably due to the intake of alcohol.²

The characteristic appearance of the person with alcoholism varies even with the time of day as well as with many other factors.¹

If the surgical condition is difficult to diagnose or the diagnosis is questionable, it is imperative that the examiner keep in mind the possibility of alcoholism. It is when this is neglected or forgotten that the condition is wrongly diagnosed and the patient allowed to follow his course precariously, often approaching a state of depression, near mania or even delirium tremens.³ There is, then, a logical reason to be aware of the possible presence of alcoholism, because trauma or elective operation, as well as minor operations, can precipitate trouble. Even more important is it to diagnose what I believe should be called concealed chronic alcoholism, for in such a case the surgical treatment must be individualized. The patient must be studied as presenting a psychologic,³ if not a medicolegal, problem.¹ He should undergo general and special routine examinations, and such examinations should be a part of the surgeon's procedure. Until further evidence has developed as to the scope of the term concealed chronic alcoholism, any case of alcoholism in which the diagnosis is not made at the time of onset of the surgical condition may be considered justly one of concealed alcoholism.

DIAGNOSIS

The diagnosis will be obtained from (a) the information offered by the patient's relatives, (b) the history related by the patient, (c) the results of the routine examination of the patient and (d) the results of the special examination of the patient, as well as of laboratory tests.

If the examiner finds the patient unnecessarily hasty, he should always impress on him and his family the importance of the questions

1 Crothers, T. D. *Inebriety. A Clinical Treatise on the Etiology, Symptomatology, Neurosis, Psychosis and Treatment and the Medico-Legal Relations*, Cincinnati, Harvey Publishing Company, 1911.

2 Iida, Y. *Influence of Aliphatic Alcohols upon the Pigment-Excreting Function of the Liver and Kidneys. A Comparison of the Effects of Aliphatic, One-Basic, Saturated Alcohols*, Jap J Gastroenterol 8 179-186 (Dec) 1936.

3 Kelly, J. A. *Post-Operative Psychoses*, Am J Obst & Gynec 59 1035, 1909.

and the need of care in uncovering all pertinent facts. Often when the physician insists on all details and explains that nothing can or will be done until the routine of taking of the history is complete, the patient will reverse his attitude and proffer information which he at first withheld. The history taking must not, however, be prolonged in an unwarranted way. The amount of questioning will vary in each case.

Methods of interrogating the patient hardly appear to call for detailed description, but because of the variability in examiners' methods, in the findings and in the cooperation of patients certain points should be emphasized.

Standard questions should be put, and they should be asked with authority. The physician must learn the exact amount of alcohol taken in a given length of time whether it was by the day, the week, the month or the year. Persistence will nearly always bring out unexpected facts.

The connotation word "routine" as applied to the examination of a patient depends on the severity and location of the lesion calling for surgical intervention. The complete routine examination, not excluding a neurologic examination includes a record of the findings from head to foot. An exact rule cannot always be followed. It is advisable to make examinations always in the same way. When the order must be changed or a part of the examination delayed repeated examinations should be regularly carried out. Methods of charting should be uniform. In some hospitals it is already a routine to make uniform records of all patients because in the past delays in taking histories and irregular charting of incomplete information have led to distressing legal difficulty.

During the entire so-called routine examination the examiner should be on the watch for evidence of concealed chronic alcoholism, especially if the history is suggestive. Education as to what to look for must vary with the examiner and the practice.

The special examination of patients suspected of alcoholism will of course be a part of the conscientious physician's routine. Eventually there should be no need to differentiate these two parts of the investigation. For the sake of emphasis I shall group certain aspects of the total examination under the head of special examination.

The special examination must be undertaken with alcoholism in mind, either at the time of the routine examination or immediately afterward. The order of examination should be uniform. The examiner may begin with the head and end with the extremities or he may use any order of search that includes all the systems that is the skin the bones and joints the circulation the respiration the digestion and the nervous system. In addition there should be a brief but conclusive summation.

of the history and findings. This will bring out considerations that might otherwise be overlooked.

The signs to look for are many. The examiner should recall that the effects of alcoholism may vary. The condition may at times be associated with or cause possibly only indirectly, the following changes: (1) premature age (gray hair, obesity and sedentary habits), (2) cutaneous changes (atrophy, venous engorgements, telangiectases, acne-like lesions, erythematous eruptions and other changes of color, such as pallor or yellowness and rarely, even purpuric changes), (3) metabolic changes, some temporary and others definite and permanent, in all probability arthritis, dermatoses not already mentioned and cardiac symptoms (if not definite cardiac disease), (4) possibly, renal and hepatic disease, diseases of the blood-forming organs or of the glands of internal secretion, also, diseases of the central nervous system as well as peripheral neural involvements, and (5) mental and moral deterioration when truly gross changes in the nervous system have not yet occurred.

Any one who wishes to question these statements may do so, but no one can deny that thousands of patients have been observed who presented many degrees of these changes with no fact available clinically to explain their conditions but the definite history of an intake of alcohol. Unfortunately the lack of total abstainers as controls for the determination of the diseases related to alcoholism prohibits final conclusions.

If one examines persons with acute alcoholism, however, one cannot deny that (a) such patients may have intense nervous exhilaration from release of the higher centers or they may have depression of such severity as to cause cyanosis affecting the metabolism of the entire body, even enough to cause death, (b) they may react to alcohol according to known variants or they may manifest tolerance—a state observed clinically though not yet demonstrated by laboratory and other scientific tests,⁴ (c) they may at times exhibit an unexplained susceptibility to alcohol.⁵

The action of alcohol appears to be incompletely understood, but this does not mean that its effects can be omitted from consideration.⁴

The special examination, then, if carefully performed, will often reveal numerous abnormalities. Many of these can be ascribed to factors other than alcoholism, but this, of course, should not exclude them from consideration.

⁴ Newman, H., and Card, J. Nature and Tolerance to Ethyl Alcohol, *J. Nerv. & Ment. Dis.* **86** 428-440 (Oct.) 1937.

⁵ (a) Silkworth, W. D. Alcoholism as a Manifestation of Allergy, *M. Rec.* **145** 249-251 (March 17) 1937. (b) Streat, L. P. A Case of Angioneurotic Edema from Alcohol, *Canad. M. A. J.* **36** 180-181 (Feb.) 1937. Crothers,¹ Ida.² Newman and Card.⁴

In the description of cases which follows the details of the histories and examinations will be instructive in pointing out ways to enhance a routine examination

As yet there is no practical or universally approved test on the result of which one may base an absolute diagnosis of chronic alcoholism and undiagnosed alcoholism is rarely mentioned in the literature. Tests for alcohol in the blood of persons under or recently under the effects of alcohol are advocated but are not yet in use in most hospitals. So far then the only tests available to the physician are tests for the chemical composition of the blood, tests for metabolic function various blood counts analyses of secretions (exclusive of their alcoholic content) and a few tests for vitamin deficiencies.

Almost any laboratory test may be indicative of disturbed function, which in turn may be partly due to the effects of alcohol. Such tests can be done when necessary to determine the presence of such conditions as disturbed metabolism anemias, nephritis and hepatitis.

A gastrointestinal series of roentgenograms taken after administration of a barium sulfate enema seems to me of value in pointing out early an abnormality of function in the digestive tract particularly stasis which is at times associated with chronic alcoholism.

Although an intelligence test may be a far cry from the surgical condition at hand and from the condition of concealed chronic alcoholism that is suspected I wish to suggest that such a test be made. The careful examiner does, as a matter of fact observe the mentality of all patients at all times, but the results are not uniform unless a regular procedure is followed. Thus under the pressure of interest in a surgical condition in the patient, the physician may not converse with him at sufficient length to notice his loss of memory for past events his inability to orient himself or his inability to add a column of figures. Whenever relatives are unaware that there is a change in the patient or are reticent about volunteering such information about him or cannot be reached for questioning it seems worth while to include the physician's opinion of

6 Dauphin P Undiagnosed Alcoholism *Marseille-med* 2 597-639 (Nov 15), 648-673 (Nov 25) 1935

7 Gettler A O and Siegel H Quantitative Isolation of Ethyl Alcohol from Tissues of Alcoholics *Am J Clin Path* 7 85-93 (Jan) 1937

8 Wright I S and Lilienthal A The Pharmacologic and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid) with Especial Reference to Its Effects on Capillary Fragility *Arch Int Med* 57 241-274 (Feb) 1936

9 Chirav, G A and Deparis M Diagnosis of Acute Hepatitis in Chronic Alcoholism by Test of Provoked Galactosuria *Arch d mal de l'app digestif* 26 481-526 (May) 1936 Guillot M and Gwan O S Inhibiting Action of Alcohol on the Action of Acetylcholine and Histamine on the Isolated Intestine of the Guinea Pig, *Compt rend Soc de biol* 125 33-35 1937

the patient's mental and moral status as one result of the special examination. I do not wish to imply that the physician should always suspect a brilliant student of dementia or a prominent executive of Korsakoff's syndrome, yet the occurrence of a sudden surgical calamity may temporarily blind the casual examiner unless definite questioning and deduction along this line are included in the special examination.

I wish to present now a few case histories in sufficient detail to illustrate the points I have mentioned. The patients were encountered in my own practice. Some, if not all, should be considered as presenting true alcoholism describable as concealed chronic alcoholism only because of the delay in the recognition of the most important facts uncovered in the histories, examinations and certain tests. A few are possibly to be considered as having true concealed chronic alcoholism.

REPORT OF CASES

CASE 1—A man aged 32 was admitted to the New York Post-Graduate Medical School and Hospital on Aug 2, 1936. The patient was a Southerner and apparently well to do.

Family History—The father died when the patient was very young. There was one brother, who was in only fair health and was a "heavy drinker." The mother was living and well, aged about 65.

Marital History—The patient had been married twice. He was divorced from the first wife and was separated from the second after seven years of marriage. There were no children.

Past History—The patient had had typhoid at the age of 13 and pleurisy at the age of 26 and at the age of 30. When he was 28 years old, the tonsils and adenoids were removed and circumcision was done. Three operations had been performed for hemorrhoids, at the ages of 24, 25 and 29. At the age of 30, he had had phlebitis in the right leg, requiring rest in bed for six weeks. The leg swelled to twice the normal size, and the condition was supposed to have been caused by repeated sprains of the right ankle, suffered while the patient, intoxicated, was playing golf in the rain.

Habits—He had smoked two and one-half packs of cigarettes a day for years. His intake of alcoholic liquor had been constant for years in slightly varying amounts, with a few intervals (months) when only beer was taken.

Occupation—The patient had never been employed except temporarily, for a few months, on one job.

Present Ailment—Pain had been present in the right leg for months and had been especially severe the last week or two. The patient had been treated for thromboangitis obliterans by diathermy, baths, suction boot and other means, without relief. He had had so much pain in the week prior to admission that he had done little but drink malt and spirituous liquors. He insisted that the leg was normal after the recovery two years before. He said he had taken no food for a week.

Physical Examination—The patient was a well nourished though somewhat ill man. He appeared to be well oriented and to realize somewhat the serious-

ness of his condition. He complained of intense pain in the right leg and made no effort to use the extremity. He guarded it from any contact even with soft blankets.

Head and Neck. The hair was somewhat untidy, although it had been recently cut, the scalp was in good condition. The skin of the face was slightly mottled with erythematous areas of slight extent. The airways of the nose were open but there was a deflection of the septum. The breath seemed alcoholic. The eyes were not remarkable though slightly bloodshot. There were tremors of the eyelids and the tongue. The teeth were dirty and discolored out of proportion to the patient's age and social station. The throat was red. The tongue was dry, clean and thick. There was a strong gag reflex. The chin was receding and the lower lip somewhat infolding along the crease, 1 cm. below the vermilion border. A short moustache covered the upper lip. The external ears were of fair color only. The skin of the face was closely shaven. The neck was not remarkable but was somewhat flabby. No lymph nodes were palpable and the thyroid was not felt. Close examination showed a somewhat rapid beat in the slightly pulsating cervical vessels.

Chest. The chest showed nothing remarkable. The muscular development was not unusual. The skin seemed flabby and there was a layer of fat over the muscles. The heart sounds were characterized by slight softness and faintness. The pulse rate varied from 96 to 110. The blood pressure was 100 systolic and 70 diastolic.

Abdomen. The abdomen was slightly obese but the only abnormal finding was muscle spasm in the lower quadrants especially above Poupart's ligament on the right side. The pulse of the right femoral artery and that of the right external iliac artery could not be made out. The genitalia were normal. Rectal examination showed spasm of the sphincter and evidence of scarring. There was slight protrusion of the rectal mucosa and the patient refused further examination than that gained by reinserting the prolapsed hemorrhoid.

Extremities. The arms were well proportioned and fairly well developed and the hand shake revealed a soft, pliable hand. The hands were moderately well cared for. The fingers were nicotine stained, and there was a tremor of the outstretched fingers. The right leg was paler than the left. It was cold and was hypersensitive throughout its length. No pulse was palpable in the femoral, popliteal, dorsalis pedis or posterior tibial vessels. The severity of the condition did not warrant oscillometric readings at this time. There were no ulcerations of the bottom of the foot along the anterior transverse arch or on the lateral side of the sole. The left leg showed diminution if not absence of the dorsalis pedis and posterior tibial pulses although the popliteal and femoral pulses were strong. The left leg was warm and except for the callus over the outside of the sole and ball of the foot showed no abnormality unless the slightly pink toes might have been considered abnormal. The return of circulation to these toes after squeezing was immediate.

Laboratory Observations.—On August 3 the red cell count was 4,880,000, the white cell count was 11,000, there were 71 per cent polymorphonuclears. The bleeding time was four minutes and the coagulation time four and one half to six minutes. A platelet count on a later date was 200,000. The nonprotein nitrogen content of the blood was 29 mg., that of urea nitrogen 7 mg., that of sugar 80 mg. and that of chloride 545 mg. per hundred cubic centimeters. The carbon dioxide-combining power was 56. The urine was acid and had a specific gravity of

1012 otherwise the results of analysis were negative. On August 7 the carbon dioxide-combining power of the blood was 48.5, the inorganic phosphate content was 17 mg. and the calcium content 11.3 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. Oscillometric readings on August 6 showed no excursion of the needle in connection with the right leg or thigh and slightly diminished excursion in connection with the left thigh and lower third of the leg. The readings for the upper and lower parts of the arms were satisfactory. The patient's blood was of group III (Jansky). The return of circulation after elevation of the right leg for two minutes required twelve seconds but on the left when observation was made of the color of the toes on August 6, the return of circulation was only slightly delayed. The pulses in the left foot were felt easily on August 7. Repeated Landis tests showed no change of temperature in the right foot after immersion of the arms in hot water (above 110 F.) for thirty minutes or more, nor sweating of the right leg below the ankle. The left leg reacted normally.

On September 8 roentgen examination of the chest showed chronic root, branch and central bronchial thickening, with moderate dilatation toward the bases of the lungs.

On September 8 an electrocardiogram showed only a fast auriculoventricular rate of 112.

On October 2 the basal metabolic rate was +26 per cent and on November 4 it was +14 per cent.

Treatment—Conservative treatment included regular diet, low protein diet, forcing of fluids, infusions of physiologic solution of sodium chloride and of 5 per cent solution of sodium chloride, transfusions of female blood, administration of vitamin concentrates, general massage, catharsis, colonic irrigations, application of dry mild heat from an electric light bulb cradle, use of infra-red rays, elevation of the legs and hanging down of the legs over the side of the bed, and therapeutic use of Landis tests. Also, typhoid vaccine fever therapy (with estradiol benzoate) and treatment with "carnacton," insulin and insulin-free pancreatic tissue extracts were tried. In addition, a daily allowance of whisky was given, and calcium lactate, sodium salicylate, spasmalgin (an opium-atropine preparation) and sodium iodide were tried. Finally bromides, phenobarbital, codeine, morphine and atropine were given before conservative treatment was abandoned, on September 5.

Operative treatment consisted of midthigh amputation of the right leg, performed by the method of enucleation on September 5, with the patient under ether anesthesia.

Postoperative treatment included administration of morphine, codeine, phenobarbital and small portions of whisky (which the patient supplemented with repeated additions from his own sources in spite of surveillance). He was discharged from the hospital on October 11, with a healed amputation stump in excellent condition.

Comment—This case contains a lesson for all surgeons who are confronted with patients who admit consumption of alcohol but appear so cooperative and so ill from their surgical condition that their faces and manners belie their true history and the condition of chronic alcoholism. The alcoholism in this patient was not difficult to diagnose except that its significance was probably underestimated until he suffered from a condition calling for surgical intervention. Every one who saw

the patient remarked after a few days of conservative treatment how much he had improved

The nurses, however, soon discovered him in lies about smoking and drinking, against orders. This was amply borne out by his subsequent misstatements to the examiners. Fortunately, the contact between the staff and the patient was sufficiently close and often repeated to engender mutual respect. It was possible, then, to get fair cooperation from the patient, considering his reputation for emotional imbalance and drunkenness.

However, after the patient recovered from the operation and the stump was healed, his cooperation lessened considerably. His desire to maintain a reasonably clean and moral life appears from reports to have faded. It is noteworthy that he spent a good many of his years in the company of the patient in case 5 under much the same conditions of self indulgence.

Summary—Every paragraph under the detailed history records observations obviously pointing to a diagnosis of alcoholism. These are supplemented by details of physiognomy and results of physical examination, as enumerated. The therapeutic administration of alcohol appeared to be helpful.

CASE 2—A man aged 41, American born of Italian parents, was admitted to the New York Post-Graduate Medical School and Hospital on Nov. 29, 1935.

Family History—The facts are irrelevant except that extreme poverty and poor home conditions prevailed during the patient's youth. The patient's father was a drunkard.

Marital History—The patient had been married eight years. His wife was strong and well. There was one son living and well.

Past History—The patient had suffered several injuries at work during a period of several years. One of these injuries consisted of multiple fractures of the ankle necessitating a period of hospitalization. The last injury had occurred within the past three years. There had been no operations with the exception of repair of the distal phalanges of the right thumb and forefinger during childhood. He recalled the usual children's diseases as having occurred without complications.

Habits—The patient admitted a variable intake of alcohol for many years and he smoked constantly. His wife amplified the story by saying he is a terrible drinker when he gets started.

Occupation—The patient was a structural steel worker.

Present Illness—In the patient's own words: "At 10 a. m. the snap of the riveting gun broke and the plunger of the gun hit my right big toe. I worked until 4 p. m. but had to stop on account of pain which I could not stand any longer."

Physical Examination—Examination revealed a nervous, highly excitable man who appeared to be in pain but was otherwise healthy and cooperative. The temperature was 97 F, the pulse rate 72 and the respiratory rate 20.

Head and Neck—The hair was thick, unruly and black, beginning to turn gray; there were no abnormalities of the eyes, nose or ears. The teeth were in

fair condition. The tongue was slightly coated. The tonsils were atrophic. The throat was not inflamed. The neck was thick and short but otherwise normal. The face was coarse and the facial features thick and heavy, the eyes were sharp and dark.

Chest. The blood pressure was 140 systolic and 90 diastolic. The chest was rounded and barrel shaped. No abnormality of the heart or of the lungs could be made out through a very thick chest wall.

Abdomen. The abdomen was obese, presenting no other abnormality, the genitalia were normal. Rectal examination was not done.

Extremities. The extremities were short, heavy and well developed. The right great toe was swollen to about one and one-half times its normal size. It was bluish at the base of the nail, and there was a slight abrasion of the skin at this point. There was abnormal motility between the distal and proximal phalanges. There was variable but slight tenderness over the tarsus, this was not definitely localized. The legs were short in proportion to the body.

Laboratory Observations.—The results of urinalysis were normal. The blood count showed red cells, 5,700,000, white cells, 10,000, hemoglobin 98 per cent, polymorphonuclears, 54 per cent. The Wassermann and Kahn reactions were negative. The nonprotein nitrogen content of the blood was 45 mg, the urea nitrogen content 152 mg and the sugar content 95 mg per hundred cubic centimeters. The roentgenogram showed a fissure fracture of the base of the distal phalanx of the right great toe, in good position.

Treatment.—Treatment consisted of application of a plaster cast from beyond the end of the toes to the midportion of the lower part of the leg for fourteen days, followed by use of an iron plate in the shoe for several weeks. Hospitalization was of two weeks' duration. The patient was allowed out of bed after the first day and was given the regular diet after the second day. Whisky was supplied on two or three occasions on the second and third days because of his extreme restlessness and irritability and also because of a rise of the temperature to 100 F, a rise of the pulse rate to 96 and my belief that he was faced with the onset of delirium tremens.

Comment.—The patient was difficult to handle from the beginning, and his suffering seemed out of proportion to his injuries. His requests to return home and start work could be met only by the application of a heavy, unwieldy cast sufficient to impress on him his helplessness and need for care. His insomnia and bad behavior in the ward would have jeopardized the healing of his fracture with any other treatment than a heavy cast, for he got up several times without permission during the first night or two and stumbled about in the dark. The high non-protein nitrogen content of the blood was determined after I had observed some edema of the left ankle several days after his admission. The patient then admitted that he had noted attacks of edema of the ankles during the last year or two, after drinking beer. It is decidedly questionable how the patient would have reacted had he not been given the two or three doses of whisky when he was most obstreperous.

Summary.—The history was suggestive of alcoholism and the presence of the condition was admirably proved by the behavior and

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physiognomy of the patient, and by the physical signs, as well as by the good results of alcoholic medication

CASE 3—A white man aged 29 was admitted to the Broad Street Hospital on Jan 20, 1937. He was seen for the first time by me twelve hours after a drinking bout, with a 4 inch (10 cm) irregular laceration and other smaller lacerations of the scalp, one stab laceration of the right forearm and numerous scratch abrasions of the body. He was completely sober and stated that he knew nothing about having been injured until he awakened in the morning and found himself bleeding from his scalp.

Family History—The father died at the age of 58 and the mother was living and well at the same age. Two sisters were living and well. One uncle aged 68, had diabetes.

Marital History—The patient had been married nine years. There were no children. He had been temporarily separated from his wife but the couple had been reunited several times.

Past History—The patient had had pneumonia at 16 and tonsillitis at 23 (requiring hospitalization) and he believed he had had measles, mumps and whooping cough, but he was not sure. There had been no operations except a repair of a laceration of the lip at the age of 14. There had been no other accidents except a fracture of the ankle at the age of 18, which had caused him no trouble since.

Habits—He had smoked more than a pack of cigarettes a day for years. His intake of liquor was variable but immoderate except during the periods when he abstained completely.

Occupation—The patient was a commission bond salesman in a large Wall Street firm.

Present Ailment—There were multiple injuries including lacerations of the scalp and of the right arm and abrasions and contusions of the body.

Physical Examination—The patient was obese appearing several years older than his age. His light blond hair was cut short and was matted with dried blood. From the expression of his face and the bloodshot eyes it appeared that he had been drinking. He was cooperative and somewhat nervous and concerned about his condition. He was completely oriented and intelligent and was impatient to be treated. The temperature was not elevated, the pulse rate was 100 and the respiratory rate 18.

Head and Neck. The scalp was lacerated with an irregularly shaped wound in the left anterior parietal region approaching the midline. This wound was at least 4 inches (10 cm) in length. There were three other small superficial lacerations of the scalp, one in the right parietal region, another in the left upper temporal region and one posteriorly in the occipital region. There was no blood in the ears, nose or mouth.

The nasal septum was deflected. The external canals in both ears were somewhat irregular in contour because of exostoses. The ear drums were retracted. The hearing in the left ear was considerably diminished. The eyes showed no abnormalities except slight redness or injection of the small vessels of the tarsal and bulbar conjunctiva. The teeth were discolored to a degree out of proportion to the patient's age and social status.

The tonsils were scarred and red from chronic infection along the anterior pillars. The submaxillary lymph nodes were palpable in a somewhat obese neck.

The features were coarse, and the patient looked like a person with chronic alcoholism.

The thyroid was not palpable. There was no stiffness or tenderness of the neck.

Chest The blood pressure was 125 systolic and 90 diastolic. The heart and lungs presented no abnormal physical signs. The skin of the chest anteriorly and posteriorly was marked by long scratch abrasions in various directions, all superficial.

Abdomen The abdomen was obese but presented no other abnormality except scratches similar to those on the chest. The genitalia were normal. Rectal examination was not done.

Extremities The limbs were fairly well developed and somewhat obese. They presented no abnormalities except for scratch abrasions on the arms. There was an avulsed stab laceration at the lateral end of the antecubital crease, at the junction of the upper part of the right arm and forearm. The edge of skin lacerated at this point was about 3 inches (7.5 cm) long, and the cut was in the shape of an acute angle with its apex pointed toward the shoulder. There were gross tremors of the outstretched hands. There was no paralysis of either hand.

Laboratory Observations—Laboratory tests, including the Wassermann and Kahn tests, showed no abnormality. The blood counts were normal. Urinalysis at the time of entrance to the hospital gave negative results except for the presence of 14 per cent sugar by the quantitative Benedict determination. Roentgenograms of the skull showed it to be normal, and the sugar content of blood taken the day after the patient's entrance into the hospital was 90 mg per hundred cubic centimeters, with the patient fasting.

Treatment—Treatment consisted in debridement and repair of the lacerations of the scalp (after careful hemostasis) and a plastic repair of the laceration of the right arm. The patient proceeded from fluids to the regular diet within three days, and except for nervousness, irritability and restlessness, which were relieved on the third night by 2 ounces (60 cc) of alcohol, he was easily handled by oral administration of amyltal and phenobarbital.

Comment—The patient when first seen (in his apartment) was hard to handle. He refused to enter the hospital until he had practically fainted in an attempt to prepare himself to undergo the suturing of his wounds at home. He could be persuaded to go to the hospital only with the promise that he could also have his tonsils removed after a day or two. In the hospital, at the end of about six days, when it was believed reasonably safe to consider a tonsillectomy, he refused this procedure. He also refused narcotics, and it is my belief that the good night's rest on the third night, after two nights of poor rest, was probably determined by the intake of a small amount of alcohol that evening.

Summary—The marital history, the habits and the recent drinking of alcohol should be emphasized. The physiognomy and some of the physical findings may be significant. As the patient refused narcotics, he was difficult to manage until whisky was given him.

CASE 4—A white man aged 43 was first seen by me on March 5, 1936.

Family History—The father died at the age of 30, of a long illness of unknown nature. The mother committed suicide at the age of 51. Two brothers were

living and well. One brother died at the age of 6 months, of unknown cause. There were no sisters. The patient's mother had been temporarily insane after childbirth and had been committed to an asylum.

Marital History—The patient had separated from his wife after several years of marriage.

Past History—The patient had had gonorrhea in 1929 with no further difficulty until there was a slight discharge from the urethra three months prior to examination. There had been a bullet in the left knee since the age of 14—an accidental injury. Roentgen examination had been done for possible ulcer at the age of 32; the patient had fasted for fourteen days and had had no pain since. He stated that it was his habit never to eat fried foods. He had been told that his appendix appeared webbed on roentgen examination. He had known of a growth on the right tonsil for a long time.

Habits—The patient had been a consistent drinker of beer since before prohibition and had "suffered slight dizziness for years and a feeling of falling." He was a heavy smoker of cigarettes.

Present Ailment—There had been nervousness over his health for several weeks. He complained of a urethral discharge which had been present for three months, of slight pain in the right side of the abdomen present for three or four days and of nocturia which occurred about once a week.

Physical Examination—The patient was a nervous, pallid, well-nourished, cooperative, intelligent and respectful man who appeared to be about the age he claimed (43); he seemed slightly and chronically ill but active and well oriented. The temperature was 99 F, the pulse rate 84 and the respiratory rate 18.

Head and Neck. The hair was slightly thin; the eyes were alert; there was no abnormality except slight lid lag. The ears were essentially normal. The nose showed deflection of the septum; the teeth were discolored, decayed and in need of immediate attention. The thyroid was palpable, small, firm and deeply placed. The submaxillary glands were palpable. There was an almond-shaped and almond-sized polyp of the right tonsil. Both tonsils were large and deeply placed and were slightly red along the anterior pillars.

Chest. The blood pressure was 130 systolic and 80 diastolic. The heart and lungs revealed no abnormality. The skin of the upper sternal region was slightly rough.

Abdomen. The abdomen was slightly obese. Rectal examination disclosed no abnormality except that the prostate was slightly enlarged and boggy but not tender. Examination of the genitalia showed a long prepuce and a moderately profuse seropurulent urethral discharge.

Extremities. There was a scar on the medial side of the left knee. There was a marked tremor of the extended fingers. The knee jerks were hyperactive.

Laboratory Observations—The Wassermann and Kahn reactions were negative.

Treatment—Therapy consisted in forcing of fluids, local hygienic treatment of the redundant prepuce and administration of bromides by mouth and of acetylsalicylic acid for the local infection in the mouth. A few days later, after roentgen study had shown that the roots of the teeth were grossly infected, the patient had several teeth extracted by a reputable dentist. Six hours after the extraction he suffered a moderately severe hemorrhage for which he had to be treated in an out-of-town hospital. Recovery after the hemorrhage was gradual but satisfactory. The patient has had further teeth extracted at intervals during the past year without mishap.

Comment—The danger of hemorrhage in a patient who may have chronic alcoholism should not be overlooked, in spite of the well known fact that both hemorrhage and infection are common in persons who have several badly infected teeth removed at once. In the case reported here, multiple extractions should not have been done without safeguarding the patient against such consequences. It is well to remember that this patient might have been given considerable comfort after the operation by the administration of a small amount of alcohol and that the anxiety aroused by the considerable hemorrhage might better have been treated prophylactically by a stay in the hospital after the extraction, which would have guaranteed a night or two of sleep under ideal conditions.

Summary—The bad family history, the suggestive marital maladjustment, the past history of the patient, his habits and his symptoms all indicated concealed chronic alcoholism, which was further to be suspected from the patient's physiognomy and behavior and from the physical findings and the course of the illness. Alcohol was not used therapeutically in this case.

CASE 5—A white man aged 36, a Southerner, was seen once, Sept 1, 1936.

Family History—The father died of pneumonia at the age of 50, the mother was living and well at the age of 50. The patient was an only son. A first cousin had thromboangitis obliterans.

Marital History—The patient was divorced after having been married for several years. He had a daughter.

Past History—The patient had had scarlet fever at the age of 16. He had had measles, mumps and jaundice as a child. At the age of 29 the tonsils had been removed because of recurrent sore throat. All the upper teeth had been extracted. Fracture of the left clavicle had occurred at the age of 30.

Habits—The patient had smoked steadily since the age of 13 and had drunk beer and liquor since the age of 17.

Occupation—He had no occupation at this time, although he had graduated from law school, passed the bar examinations, and practiced law a short time in his home town.

Present Ailment—The patient complained that he had suffered from pain in the calves for one year and from burning of the feet for many years, with relief on removal of the shoes. He had had difficulty with the feet when in the army. He described an intermittent feeling of fatigue and heaviness, without cramps but with some ache above the knees and in the calves during the last year. This was immediately relieved by rest.

Physical Examination—The patient was a hollow-eyed brunet of good education, thin but fairly healthy. The temperature was normal. The pulse rate was 90 and the respiratory rate 18.

Head and Neck—There were no abnormalities of the head and neck with the exception of chronic nasopharyngitis. The upper teeth had been removed. The remaining teeth were in poor condition. The tonsils had been removed.

Chest The blood pressure was 120 systolic and 80 diastolic. The heart and lungs presented no abnormalities.

Abdomen The abdomen was soft and flabby, not obese but slightly prominent as compared with a somewhat flat chest. The liver, spleen and kidneys were not palpably enlarged. The genitalia were normal. Rectal examination was not done.

Extremities The arms were normal. The legs were well developed though somewhat thin. The popliteal dorsalis pedis and posterior tibial pulses were not as easily felt on the left as on the right. Especially was this true of the dorsalis pedis pulse, which at times was difficult to make out at all.

A tentative diagnosis of thromboangitis obliterans was made and the patient was advised to discontinue smoking. He was instructed to return for further diagnostic tests and the outlining of treatment. He was afterward seen nonprofessionally when he admitted that he could not stop smoking and that he had done considerable heavy drinking. He did not think he would bother with further diagnosis and treatment.

Comment—It is interesting that this patient showed the clinical symptoms of early arteritis obliterans and gave some evidence of the disease. Significance may or may not be attached to his long association with the patient in case 1 (since childhood) and to the fact that he had a first cousin with a circulatory difficulty of the legs, which had been pronounced thromboangitis obliterans. All 3 of these persons were young men about the same age (in the thirties) who had led a similar life in the same town. At the time of writing the patient seems likely to follow a course similar to that of the patient in case 1.

Summary—The similarity to case 1 is obvious—marital difficulties, a past history of consumption of much alcohol and the history and findings of circulatory disease of the extremities. The lack of psychic stamina, as shown by the patient's lack of interest in his own future when his friend had recently lost a leg from a disease perhaps similar to his own, gives an idea of the lack of hope in some of the cases of this type. The family past marital and other history was indicative as were the ailments presented, the physical findings, the known pathologic course and the patient's admitted inability to abstain from alcohol. Alcohol was not prescribed in this case.

CASE 6—A woman aged 61 was first seen by me about 1 a. m. on Jan. 24, 1935.

Family History—The family history was not detailed but the facts given were essentially irrelevant.

Marital History—The patient had been married approximately thirty-five years. She had had no children.

Past History—She had had disease of the gallbladder four or five years prior to examination. This was cured with conservative treatment.

Occupation—The patient was a housewife who had done literary work.

Habits—There was no history of intake of alcohol.

Present Illness—The patient complained of loss of function, pain, swelling and abnormal mobility of the upper end of the left arm and shoulder. She had

received an injury while riding on a railroad train the same evening, January 23, about 7 p. m., when she was thrown out of her seat by the sudden jolt of the car. The patient refused first aid treatment and took a car back to the city of New York from several miles out in New Jersey, where the accident happened. She had had no food, medication or treatment up to the time I saw her, at 1 a. m.

Physical Examination—The patient was an obese woman, nervous, pallid and in pain. She held her left shoulder with her right hand. Examination further than that necessary to determine abnormal mobility and distortion of the left shoulder joint was postponed until she was taken to the hospital.

Head and Neck The hair was gray and somewhat thin. There was tenderness of the scalp over the occipital end and the parietal region. The ears were essentially normal. The upper and lower eyelids were puffy, and the patient complained of difficulty in keeping her eyes open. The pupils reacted poorly to light, accommodation was poor, there were some nystagmoid movements on looking to either side. The nose was thick and bulbous, the airways were fairly good. The gag reflex was strong. Many of the teeth had been removed. The tonsils showed no abnormality. The neck was obese and short.

Chest The blood pressure was 170 systolic and 100 diastolic. The pulse rate was 100. No abnormalities of the heart or lungs were noted.

Abdomen The abdomen was not examined particularly except for tenderness. Obesity prohibited palpation of any of the abdominal organs.

Extremities The legs were obese, there were minor bruises of the lower part of the left leg. The knee jerks were variable. The right arm was normal, the left arm was swollen at the shoulder. There was abnormal mobility at the upper end of the left humerus, with crepitus and tenderness beneath the deltoid muscle. Motion at the elbow and wrist was normal. There was no nerve palsy.

Laboratory Observations—A roentgenogram showed two lines of fracture of the left shoulder joint, involving the surgical neck and greater tuberosity of the upper end of the left humerus. Blood counts and urinalysis revealed nothing relevant.

Treatment—Rest in bed, sedatives, light diet, and strapping and sling were used. Difficulty was encountered with the patient, especially after twenty-four hours, because of her nervousness, irritability, insomnia and general complaints of numerous kinds. She did not appear to improve even after a consultant was called, and she asked for a consultant of her own choice a few days later. This one advised the same treatment but immediately suggested that alcohol be prescribed at regular intervals. Physical therapy and early motion brought about an excellent result in the arm, but the patient's general condition was poor and her behavior untrustworthy for many months after the injury. She was seen by many physicians after her original treatment, which she followed out until March 22.

Comment—Because of the patient's advanced years, marked obesity and nervous temperament she was difficult to handle. It is questionable how she would have done had she not been given alcohol daily at the suggestion of the second consultant, about a week after the injury. It was the opinion of this consultant that her denial of the intake of liquor was offset by her face, which could be probably characterized as coarsened and somewhat typical of the addict to alcoholic liquor.

Summary—This case illustrates the advantage of complete history taking and examination. The past history and other data were of little

help. The outstanding characteristics of this patient were her coarse features, bad behavior and obesity. Alcohol was suggested by a senior consultant after only a moment's sight of the patient. Her course was satisfactory thereafter, although the handling of this patient was always a problem.

CASE 7—A man aged 49 was first seen by me on Sept. 29, 1934.

The family history and the past history of the patient were not recorded.

Marital History—The patient was not married.

Occupation—He was in the advertising business.

Habits—He had been a heavy drinker and smoker for many years.

Present Ailment—There was loss of function of the left elbow since the patient fell in the bathtub on the day before examination. Pain on motion of the left elbow was noticed.

Physical Examination—The patient was a rotund, large, obese, red-faced man who appeared nervous.

Head and Neck—No gross abnormalities were noted except coarsening of the features in addition to the high complexion. The neck was obese and short.

Chest and Abdomen—Examination of the chest and abdomen was not made as the patient was ambulatory and there was no opportunity to carry out this examination.

Extremities—The legs were not examined. The left arm appeared normal in size except for slight swelling around the elbow. There was no abnormal position of any of the bones of the arm. The patient flexed the arm to an acute angle of about 80 degrees with considerable difficulty and allowed further flexion to an acute angle only after considerable argument in spite of explanations and reasons for the need of this treatment.

Roentgen Examination—The roentgenogram was not absolutely diagnostic but was suggestive of a chipped fracture of the medial epicondyle without displacement.

Treatment—The patient was instructed to keep the arm acutely flexed for at least two weeks. Instead he consulted other physicians after a few days who subjected him to physical therapy for two months before he recovered the use of his elbow.

Comment—The patient was known to be chronically alcoholic and his word was often untrustworthy. The fact that seven different physicians were consulted and the patient's own remarks a year or two later about the "jovride he went on with all the doctors" indicate the difficulty of managing this type of patient even if alcohol is prescribed.

Summary—No further comment seems necessary except to emphasize the fact that only the most untrustworthy behavior may be expected of alcoholic patients in spite of seemingly faithful promises as in this case.

CASE 8—A white man aged 36 was first seen by me on Oct. 15, 1936. He was admitted to the New York Post Graduate Medical School and Hospital on October 27.

Family History—Most of the facts were irrelevant. The father was known to be diabetic at the age of 80.

Marital History—The patient was divorced from his first wife, one son by the first marriage was living and well. The patient was living with his second wife. They had been married four years. There was one daughter by this marriage living and well.

Past History—The patient had had gonorrhea over ten years previously. Two plastic operations had been performed on the nose within ten years.

Occupation—The patient was a musician and arranger.

Habits—He had partaken of liquor in variable but often large amounts for several years.

Present Ailment—Pain in the right inguinal region had been present for four days. The only associated complaint was questionable a slight urethral discharge a few days previously, which he attributed to overactive intercourse. He said that there had been a slight blister on one of the toes of his right foot several days before that, which was now healed. His general health had been good.

Physical Examination—The patient was an obese, pale man of about the age stated, who appeared to be somewhat apprehensive but generally in good health. The temperature was 99 F and the pulse rate 88. The respiratory rate was 10.

Head and Neck—The hair was reddish, long and worn smoothed close to the head. The eyes, ears and mouth presented no abnormalities. The nose was shortened, the airways narrowed and the bridge thickened. The nose was slightly aquiline.

Chest—The blood pressure was 130 systolic and 85 diastolic. The chest was somewhat obese. The heart and lungs presented no signs of abnormality.

Abdomen—The liver, spleen and kidneys were not felt. There was a small indirect inguinal hernia on the left side, easily reducible. On the right side the internal inguinal ring was relaxed, but no impulse was felt on coughing. There was an egg-shaped inguinal lymph node on the right side, deeply placed just above Poupart's ligament. It was acutely tender, and the skin over it was freely movable. The genitalia showed no evidence of any lesion. The prepuce was redundant but not inflamed. There was no urethral discharge.

Extremities—The arms were normal. The legs were well developed. There was no evidence of lesion on either foot. The mass in the right inguinal region enlarged continuously until October 27.

Laboratory Tests—The urine was essentially normal.

Treatment—Therapy was conservative until October 27, at which time the patient was removed to the hospital, and a large deep inguinal abscess on the right was incised and drained with the patient under ethylene anesthesia. Wet dressings and heat were applied to the wound. It was practically healed at the end of two months, at which time he was sufficiently well to go to another state and begin a new job. The wound was not completely healed, and in February 1937 it required cauterization of some granulations by a physician in another state. It healed completely shortly afterward and has remained healed to date.

Comment—This patient was difficult to handle because of the chronicity and nature of his ailment. He was advised that alcohol might quiet his nerves. Alcohol was given on one or two occasions during his stay in the hospital, when he appeared to be most apprehensive. It is difficult to be sure but it is my feeling that a large part of this patient's nervousness and irritability could be traced to his previous

intake of alcohol. The patient's general good health and urgent need to recover so as to be able to provide for his family probably aided the rather fortunate outcome. In a patient with less intelligence or willingness to cooperate the same surgical condition in the face of the definite if irregular alcoholic history might have had a different outcome.

Summary—This patient suffered a long-drawn-out siege from a massive deep inguinal abscess. The past history, the habits and the marital and social history might have been suggestive of concealed chronic alcoholism. The exceedingly nervous attitude, the physical findings, the physiognomy and the actions of the patient in the hospital confirmed the diagnosis. He was apparently aided by the small amounts of whisky given him on a few occasions.

GENERAL COMMENT

The pathic person can be recognized at the time of the first examination if there is much disagreement between the history related by the patient and that furnished by others on questioning. It is a fact that in the case of the patient with a condition requiring surgical treatment who denies, understates or conceals his alcoholic habits an unusual series of events often follows.

First, he will be found sooner or later to be untrustworthy. His word cannot be depended on. Second, complications or sequelae may occur that commonly do not occur in the case of the abstainer. Third, there will often be at some time in the course of his condition evidence of loss of cerebral stamina. A better way to express this would be to say that his nervous system may show instability at various points. The higher or the lower centers or both may show function completely different from that observed in most abstainers.¹⁰

The thousand and one ways by which a physician may gain objective signs of concealed alcoholism are often forgotten.¹¹ The simplest reason for this lies in the comparative superficiality of most routine clinical and even laboratory examinations of the patient with a condition calling

10 Knight, R. P. *Psychodynamics of Chronic Alcoholism* *J. Nerv. & Ment. Dis.* **86** 538-548 (Nov.) 1937.

11 (a) Cowles, E. S. *A New Pathology and Treatment of Chronic Alcoholism*, *M. J. & Rec.* **133** 417-421 (May 6) 1931. (b) Villaret, M. *Justin Besançon*, L. and Klotz, H. P. *Fatty Degenerative Hepatitis as Prevailing Hepatic Lesion in Alcoholic Polyneuritis*, *Bull. et mem. Soc. med. d'hop. de Paris* **52** 1159-1162 (July 13) 1936. (c) Bier, H. L. *Dermatitis of the Eyelid Due to Alcohol*, *Arch. Dermat. & Syph.* **35** 291 (Feb.) 1937. (d) Bronville, H. and Titeca, J. *Abrupt Abstinence from Alcohol as a Cause of Delirium Tremens*, *Twenty-Two Cases*, *J. belge de neurol. et de psychiat.* **37** 135-154 (March) 1937. (e) Bersin, T., Lanber, J. J. and Nuziger, H. *Effect of Anesthesia and Operation on Vitamin C Metabolism*, *Klin. Wchnschr.* **16** 1272-1274 (Sept. 11) 1937. Crothers,¹ Knight,¹⁰ Kelly.³

for surgical intervention. It is not customary to apply any test which measures the psychic stamina or the functional state of the nervous system. Still less commonly is it a practice to make any test of the blood to determine even acute alcoholism.⁷ No consideration is given to such a test for patients with chronic alcoholism, because alcohol is so quickly eliminated from the body. Absolute lack of any clinical or laboratory test for unsuspected or concealed alcoholism makes a scientific approach to the whole subject at the present time practically impossible. Since alcohol is considered often in the same light as an anesthetic, vitamins C and B are worthy of consideration (Bersin and his associates)¹² Wright and Lilienfeld⁸ and others¹³ indicated latent deficiencies and need for increased vitamin intake. Anesthesia, infection and operation seem obvious¹⁴ indications for such therapy.

Psychiatry has furnished the greatest contribution to physicians' knowledge of the intellectual state associated with both acute and chronic alcoholism. Many phases of functional mental disease have been at times related or at least attributed to either direct or familial intake of alcohol.¹

In spite of all this, the surgeon repeatedly has had bad experiences with patients suffering from alcoholism of all types, especially those with concealed chronic alcoholism, because of the lack of a satisfactory clinical or laboratory test for the condition.

Occurrence—Concealed chronic alcoholism is characterized by its occurrence usually in persons over the age of 18. The upper age limit is indefinite, but probably the condition is seldom seen in patients over 75. These extremes may seem extraordinary, but they can be explained.

There are no figures to indicate how many of the population have ever acquired a taste for alcoholic drinks, how many are absolute abstainers and how many may be considered more or less constant users of alcohol. Since some line must be drawn to differentiate the abstainer from the patient with concealed chronic alcoholism, true chronic alcoholism or any of the borderline conditions between these, practical if arbitrary rules must be set down.

True chronic alcoholism, in my opinion, may be considered to affect that person who is known to have consumed alcoholic liquors during at

12 Leriche, R. Hormonal Regulations in Surgery, *Liege med* 30 876-886 (July 25) 1937

13 (a) Lauber, J. J. Vitamin Therapy in Surgical Diseases, *Med Wch* 11 415-420 (March 27) 1937. (b) Bridges, M. A. Pre- and Postoperative Nutritional Regimen. Proposed Five Point Schema, *New York State J Med* 37 2009-2012 (Dec 1) 1937

14 (a) Wechsler, I. S., Jervis, G. A., and Potts, J. D. Experimental Study of Alcoholism and Vitamin B Deficiency in Monkeys, *Bull Neurol Inst New York* 5 453-475 (Aug) 1936. (b) Jolliffe, N., and Colbert, C. N. Etiology of Polyneuritis in Addict, *J A M A* 107 642-647 (Aug 29) 1936

least a year, daily, weekly or monthly, not more than ten years previous to the time of examination. It is rare then, to consider a man as having true chronic alcoholism if he has not in the ten years previous to the time of examination consumed alcohol in moderate quantities for longer than one year.

More commonly true chronic alcoholism should be diagnosed if the patient partook of any form of liquor regularly for years, although he may not have tasted even beer for fifteen years.

Most commonly true chronic alcoholism should be readily recognized in a patient who admits years of variable alcoholic intake up to the present even if the intake is small or has occurred at intervals of as much as five years.

A chronically alcoholic person, then, should be considered as one who has had minimum habituation to alcohol in small quantities for as long as a few days only, or if at any time of his life he was given to a moderate intake of alcohol for at least a year even if this occurred only once within a period of ten years. Conversely, a man who took only minute quantities of alcohol during one year within a past period of ten years probably should not be considered as having chronic alcoholism.

Concealed chronic alcoholism should be recognized in the person who has become inebriated more than three times in his life. Psychology has demonstrated that often the doing of an act three times makes it a habit, no matter how seldom that habit is manifested. It is probable, then, that a patient admitting inebriation three times in his life is chronically alcoholic, whether by habit or by minute physical change. Conversely, again, it is probably safe to absolve a person of true chronic alcoholism if strong evidence can be found to indicate inebriation on fewer than three occasions in the event that there has been no intake of alcohol except on these occasions.

There is no need to describe the symptoms of what should be defined as acute alcoholism. These are all too well known. When doubtful they merge into symptoms of true chronic alcoholism.

One or two borderline examples might be mentioned. A person was accustomed during a period of two years to accepting a sip of liquor when entertained at the homes of friends or in public but has not tasted even beer or wine for twelve years. This person probably should not be classified as chronically alcoholic. If however this condition had existed up to the present instead of twelve years ago he would be chronically alcoholic according to my classification.

Another case might be that of a person who admits having been inebriated half a dozen times in his life but who has not tasted any kind of liquor in fifteen years. I believe the condition of such a patient is concealed chronic alcoholism. The pattern for addiction to alcohol

or the likelihood of specific sensitization, is long buried in the past but can be redeveloped quickly, as in the case of a person with true chronic alcoholism

Still further, the person who has taken alcoholic medicine at regular intervals for the relief of recurring pain and discomfort, for example, at the onset of recurring common colds or painful menstrual periods, is in my opinion a patient with concealed chronic alcoholism

It is not my purpose to say that most of the population are afflicted with true chronic alcoholism, but rather to point out that many may be considered so, or at least potentially so, if their history approaches that set forth here as the history of the patient with true chronic alcoholism and if, in addition, they are suffering from a condition demanding even mild surgical treatment

By this I mean to say that a great many patients are surgically treated every day who never are suspected of tolerance to alcohol or of need of it under stress, in "shock" or when undergoing operation. There are many such persons who on psychic or physical stimulation may be precipitated into the mental state of the alcoholic addict at his worst.¹⁵ Whereas many may wish to omit completely the moral and ethical considerations with regard to true chronic alcoholism, it is essential for all physicians to try to diagnose the condition and recognize the need for prophylactic as well as active treatment when there is an accompanying surgical state. Vitamin replenishment is always advisable, especially as concerns vitamins B and C. Opinions vary about completely omitting alcohol.¹⁶

Any number of predisposing factors besides an imminent or an emergency surgical condition can produce a recrudescence of concealed chronic alcoholism to an obvious state of alcoholism, with only a small alcoholic intake or none at all. These include fatigue, bad hygiene, overwork, lack of rest, recreation or sunlight, overindulgence in tobacco, coffee, tea or other nonalcoholic stimulants, indulgence in narcotics, poor heredity,¹⁵ bad environment, emotional instability from whatever cause, and organic and functional diseases of all kinds.¹⁷

Physical Findings—At the completion of the patient's history the examiner will suspect, or nearly rule out, the probability of concealed chronic alcoholism

The objective findings of concealed chronic alcoholism include all positive data obtained from the history as related by the patient and

15 Sereghy, E, and Marcinkievics, A. Importance of Vital Resistance in Surgery, *Orvosi hetil* **80** 815-818 (Aug 29), 842-845 (Sept 5) 1936. Kelly Silkworth^{5a} Knight¹⁰ Baonville and Titica^{11d}

16 Cowles^{11a} Silkworth^{5a}

17 Carroll, F D. "Alcohol" Amblyopia Pellagra Polineuritis. Report of Ten Cases, *Arch Ophth* **16** 919-926 (Dec) 1936

his relatives and as indicated by the classification just described. They also include data which can be obtained at the time of routine physical examination. In some cases the findings are limited to responses from the nervous system, obtained either by observation or by questions and answers. In other cases data are obtained by physical examination by neurologic examination and by certain laboratory tests.

Exclusive of the results of the usual physical examination certain evidence can be gathered which may help to classify the condition. A patient who avoids looking the examiner straight in the eye on direct questioning is to be suspected of this condition. When such avoidance occurs repeatedly even after one becomes fairly well acquainted with the patient, it may be taken as favoring a diagnosis of alcoholism.

A patient who cannot sit still or keep his hands still or who appears generally irritable, also presents possibly contributory indications. Other suggestive phenomena include the following with due consideration for extenuating circumstances in the individual case: (a) exaggerated speech, affectation or variability of talk, (b) any behavior in speech, looks, talk or locomotion which seems to indicate that the patient is ill at ease, (c) needless repetition on the patient's part of any part of the history or conversation between him and the physician, (d) the inability of the patient to exhibit normal psychic, intellectual, moral and physical control during times of suggestion by the physician examining him, for example when he shows repeated and apparently embarrassed avoidance of direct answers to subtly reintroduced questions.

Unwarranted or false cynicism which does not appear to be explained by the patient's education or known habits or the discovery that he is in a stratum of society, financial condition or professional standing greatly out of proportion to his appearance or to his known past ability should be considered indicative.

A complete physical examination is necessary to indicate many of the objective signs of true or concealed chronic alcoholism. Many of the positive signs duplicate some of those partly diagnostic of numerous diseases of all kinds.

I shall list the positive ones as though they occurred in an otherwise normal person not suffering from any definite functional disease of the nervous system from any metabolic disorder or from any systemic disease other than the condition requiring surgical attention.

First are the signs from an examination of the head and neck: an overanxious expression of the face, increased flushing of the skin, signs of premature age such as gray hair and changes in the skin, deep wrinkles, cutaneous blemishes or sometimes pallor not explained by the other habits of the patient. Sometimes the appearance of the face entirely belies the existing condition yet that condition can be recognized by a fleeting expression of emotion not explained by what the patient

or the examiner is doing, often a patient will look upright and serious and utter exactly contrary remarks. At other times he may look jovial, peaceful and contented while making a statement completely at variance with this facial expression. A repetition of these phenomena several times during a physical examination is sometimes of strong diagnostic significance. In the same way, otherwise unexplained emotional upsets should be taken into account.

Observation of the neck may show pulsation not borne out in other expected signs of hyperthyroidism or of circulatory or nervous disease.

Although the finding may not be altogether reliable, disproportion between the size of the neck and that of the head may be a point to consider. A patient may look as though his head did not fit on his shoulders and no explanation is found in heredity or habit. Here a close search for the reason has revealed the condition under discussion.

This same incongruity between the features—nose, eyes, mouth, ears and hair—has been observed by me in patients of this type in whom there was no other condition to explain it.

Extremes of regularity of features and good proportion between head and neck also are seen commonly. But there is something so obviously present in the facial expression and the way the head is carried that it is possible to say that the patient has or has not good character.

There is a type of face, seen in both males and females, which conforms to no set rule, in which there appears at times or even all the time to be something that should not be there, or something not there that should be there. Some persons repel by their facial expression, as though they withdrew from the circle of others present. These same persons can consciously or unconsciously attract by some vague change in their expression. All things being equal, however, it is significant when a patient seems distant or suddenly gives some obscure sign in his facial expression that he is once more "with us" or receptive of what is said to him. Briefly, this change in facial expression or in "atmosphere" which cannot be traced to definite poses or movements can sometimes be seen to occur several times during the examination of a patient of the type described as having concealed chronic alcoholism. Some of these patients may be said to smile without really smiling or to laugh without really laughing. Others show nothing more than a strange clouding of expression, which may be only momentary but is often repeated. The gaging of these details will be difficult for an examiner who judges his patient too early, too severely or unjustly or neglects to ask for important facts.

What I have just said applies also to the patient in whom one "feels" a distinct lack of confidence. Sometimes all efforts will be futile and

nothing the physician can do will ever establish complete "contact" with the patient. There are great differences in the powers of observation of different examiners. This is no reason to exclude admission of the fact that it is possible to observe strange unexplained changes in facial expression on some patients, or that one may recognize incongruities not explainable on the basis of organic or functional disease.

Examination of the chest and abdomen cannot be accurately separated from that of the extremities. It is true, as well that it is physically impossible to particularize the impression obtained from the entire body. A few suggestions may be fitting however, regarding the chest and abdomen. Great disproportion between the size of the thorax and that of the abdomen in regard to length of the axis of the spinal cord can signify either great 'strength of character' or marked 'weakness'. Either of these can be interpreted in the individual case to predispose toward or to exclude the consideration of concealed chronic alcoholism.

Failure of clinical examination to demonstrate disease of the respiratory tract does not exclude its presence. Laboratory aid must be employed. Presuming that laboratory aid is immediately available and that it is possible to exclude organic disease and cardiac instability of any kind, any change in the respiratory rate or in the pulse rate to considerably above normal may have significance. This often occurs reflexly on impulses from the central nervous system unexplained otherwise than by chronic alcoholism. These abnormal channels are often out of reach of suggestion or of appeal to the patient to try to calm himself. I acknowledge that many possible direct and indirect factors may initiate changes in the respiratory rate and the pulse rate. One must exclude any condition except the condition requiring surgical treatment and concealed chronic alcoholism, as though all other diseases or disturbances had already been proved absent by repeated examinations, laboratory tests and lack of proof of competent cause.

Increase in the respiratory rate if the chest (including the heart) is otherwise normal should furnish a clue to reflex stimulation of the respiratory center from some undiscovered cause. This cause may be concealed chronic alcoholism. Obviously exceptional care must be taken in ruling out other likely reasons for the condition calling for surgical intervention may itself bear a close relation to a rapid pulse rate or to deep respirations.

Gross disproportion with regard to the distribution of fat in the chest and the abdomen may furnish contributory evidence. The case of the prematurely portly but otherwise normally proportioned man may be a good example. There may be a redundancy of the abdomen or other fat deposits which appear to be out of proportion to the patient's

age or endocrine makeup. When this disproportion is sensed as gross without the examiner knowing exactly why, even when there are endocrine disturbances apparently not of long standing, a connection with alcoholism may be imagined. Absolute proof may be absent. The cause of such incongruity I do not profess to know, but the recognition of it is possible, and when it is properly associated with the many other identification marks it becomes a valuable sign.

The physical characteristics of a body obviously indulged and abused are naturally altered in many ways, especially over the thorax and abdomen. Here, as elsewhere, heredity, environment, habit and use determine the particular aspect of much that can be seen on physical examination.

If the data from a study of the patient's habits, environment, development and occupation are insufficient to explain abnormal thoracic and lumbar curvatures, these departures from normal may or may not be explained on the basis of disease. When these curves appear, to accompany other abnormal and inexplicable findings, the patient may be classified as potentially a victim of concealed chronic alcoholism.

Such close contiguity exists between many of these unexplained abnormalities and organic changes of hitherto explained cause that it will be difficult for me to prove my contentions.

Examination of the extremities may afford little of diagnostic evidence beyond that which is simply contributory to the already admitted variables. Again, it is believed that unusual characteristics of the arms, hands or fingers may give reason to suspect alcoholism. Sometimes a man's hands will appear soft and flabby, even with lack of care. Perhaps, the influence of environment and occupation aside, there is a relation between the firmness of the hand at the junction of the metacarpals and first phalanges and the qualities of determination, firmness, strength, regular habits and solidarity. It is probable that hereditary influences may be responsible for such firmness. This structural characteristic of the hand is best demonstrated when the examiner shakes hands with the patient and asks the patient to relax his hand. The hand may feel like flabby, inanimate meat or may be firm, inflexible, solid and non-relaxable. When this strong hand, that is, a hand characterized by inflexibility during forced relaxation, is encountered in addition to other completely satisfactory characteristics all the way through the physical examination and history, there is little likelihood of concealed chronic alcoholism. The opposite condition of the hands after exclusion of hereditary, developmental, occupational or environmental predispositions, may indicate concealed chronic alcoholism. It is strange also, but true, that grossly stiff, inflexible, rough hands may be particularly noticeable.

in contrast to the rest of the patient's physical characteristics. Paradoxically, this finding also may suggest the diagnosis of concealed chronic alcoholism.

It is probable that truly great disproportions in the appearance of the hands especially in texture and flexibility, length of digits and breadth and girth should be remembered among the details one should look for in compiling a list of unanswerable or little understood physical findings which when totaled from the entire examination may help in the diagnosis.

The same may be said of the legs, the arms and the feet. Examination of any patient completely naked makes the task slightly easier, for a person may seem much more perfectly proportioned without clothes than he does fully dressed. Another may appear almost weird, with disproportionately large hands and shriveled legs. Another may have an otherwise unexplained center of balance or pose, as he stands, which, in addition to a strangely flat region over the buttocks, seems decidedly incongruous in the presence of large shoulders and large knees and ankles. None of these characteristics is likely to be thought of in connection with alcoholism unless the examiner tries to catalogue the detailed observations and to exclude other obviously possible causes for each finding.

A few great studies have been made of races, types, figures, measurements, features and general racial physical characteristics, but not many practical specific genetic conclusions have been formulated. Certainly they are not generally appreciated. The task of bringing such a work to culmination must be almost endless. The problem under discussion is even more complex.

Let it be supposed, however, that one is able to discover in the patient several positive and otherwise unexplained incongruities, abnormalities or distortions of action, of consistency or of measurement and perspective. There should be no objection to the application of several of these positive 'hints' toward the solution of a most difficult problem in diagnosis. The physician is limited only by the quality and extent first, of his education and second, of his powers of reasoning and ability to observe with all the senses delicately integrated. In addition there must be a positive attempt to employ the so-called sixth sense, a higher or more refined sense than the recognized senses of touch, smell, taste, sight and hearing.

There can be no doubt that it is possible for some other sense to supersede these recognized senses, if for no other reason than that the absence of one sense has sharpened one of the other remaining senses to such an extent, for instance, that a "blind man can see." I may

refer also to the psychologic studies in extrasensory perception recently performed at Duke University

Of course, many, if not all, physical characteristics may be the sum total of results of interplay among the endocrine glands.¹² Reason does not allow one to exclude these glands from consideration. With some training, it may be possible to remember certain outstanding endocrine markings, but the number of possibilities is unlimited because of the polymorphous heredity of human beings and the already known and numerous variables in the classification of the endocrine glands and their functions.

Further, the significance of seemingly outstanding characteristics of the patient must often be minimized in the face of stronger controversial evidence. If, for example, one should observe closely a woman who is obese and appears summarily to suffer from pituitary, ovarian and hypothyroid disease or from imbalance among the indicated glands, one may find that her body functions excellently as a whole. She may have no subjective symptoms and yet may exhibit many departures from normal. She may have been productive of children, a good mother. Her abilities as a business manager and housewife may be unexcelled. She may by nature be constantly good and even-tempered. It is best, however, to record her "faults" even though they do not seem to be associated with the slightest incongruity of physical, mental, intellectual, social or moral life. If she later undergoes operation, one may be forewarned, at any rate, even though she has never shown other findings or history suggestive of concealed chronic alcoholism.

In conclusion, it is best to "size up" the patient from the point of view of every characteristic one can determine from him before making a direct diagnosis of concealed chronic alcoholism. History, physical examination and special examination for incongruities of all types must be made. Just as some one once said that "ugly people do ugly things," so some one has said as well that "handsome is as handsome does" and that "beauty is skin deep."

From the point of view of the physical proportions and characteristics alone, it is well to try, from the recording of the history and general observations up to the end of the detailed physical examination, to correlate, as one proceeds, all the data possible, using one's powers of observation and senses as though they were a fine sieve, able to sift out what would be missed by habitual neglect of the many details mentioned.

I fully realize the need of apologizing if what has been written, all too vaguely, appears ill considered or unsoundly formulated. Perhaps some of the ideas are clouded by fogs not yet cleared away by scientific investigation and exact terminology.

CONCLUSIONS

In many surgical patients who have in the past indulged in a variable intake of alcohol there appears to be a condition often unrecognized, which I should like to call concealed chronic alcoholism.

Treatment consists in appreciating the importance of the condition early in the course of surgical treatment and in the prescription of alcohol in addition to the commonly used sedatives before dangerous depression or complications have set in. Vitamin medication is indicated preoperatively and postoperatively.

A new and arbitrary (but indicated) rule of including in the first diagnosis of the condition of the surgical patient an opinion as to the possibility that concealed chronic alcoholism (or a tendency toward alcoholism) is present would guarantee the patient a safer course during his stay in the hospital.

Much can be learned from a patient as to the possible presence of concealed chronic alcoholism by a careful recording of detailed histories, a complete physical examination and close observation for changes in physiognomy and general physical appearance also by a careful noting of numerous incongruities, various endocrine activities and evidences of mental and emotional instability. A brief summary of all such positive findings should be entered on each patient's chart. The surgeon should consider the possible role of alcohol in every case he observes.

SUMMARY

A vague feeling that surgeons often neglect to consider chronic alcoholism as sufficiently significant in any surgical case until the patient has nervous symptoms and depression, often bordering on mania or other complications has prompted the recording of a surgeon's impression of what he has chosen to call concealed chronic alcoholism a term which applies particularly to patients who are actually chronically alcoholic but whose condition often goes unrecognized.

Eight detailed histories of patients treated personally—all but 2 of whom were aided by small doses of alcohol—are included in this article.

A discussion and description of fine points in diagnosis as well as a hint about 'extrasensory perception' of symptoms of concealed chronic alcoholism, are included and offered with extreme caution as to their complete reliability.

PERIPHERAL VASCULAR STATUS OF ONE HUNDRED UNSELECTED PATIENTS WITH DIABETES

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AND

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The relation between diabetes and the occurrence of peripheral occlusive arterial disease has been the subject of a voluminous literature. It is not our purpose to review the many articles on this subject. It is sufficient to point out the existence of a number of conflicting opinions which are difficult to correlate.

There are those who hold that there is a definite causal relation between diabetes and peripheral arterial disease. Hallock¹ stated "The diabetic state either initiates early or accelerates the development of premature arteriosclerosis in the young adult." One finds statements such as that of Ruprecht² "As a general rule, regardless of the youth of the patient, a diabetes of 5 years or more duration will produce arteriosclerosis." Others consider that the increase of arteriosclerosis in diabetic persons is due to neglect of diabetic treatment. Bowen,³ on the basis of roentgenologic studies of extremities over a period of years, stated that the development of severe vascular pathologic conditions in diabetic patients requires several years of neglect of the diabetes. Joslin⁴ expressed the conviction that arteriosclerosis is secondary to diabetes and that the severity of the former is in direct proportion to the duration of the latter. Allbutt⁵ noted many instances of sclerotic

From the Clinic of Sympathetic and Vascular Surgery, Mount Zion Hospital

1 Hallock, P. Arteriosclerosis in Young Diabetics, *Am J M Sc* **192** 371, 1936

2 Ruprecht, A. Diabetes Mellitus in Its Relation to Vascular Disease. *J Oklahoma M A* **26** 284, 1938

3 Bowen, B D, Koenig, E C, and Viele, A. A Study of the Lower Extremities in Diabetes as Compared with Non-Diabetic States from the Standpoint of X-Ray Findings, with Particular Reference to the Relationship of Arteriosclerosis and Diabetes, *Bull Buffalo Gen Hosp* **2** 35, 1924. Bowen, B D, and Koenig, E C. Arteriosclerosis and Diabetes Including a Roentgenological Study of the Lower Extremities, *ibid* **5** 31, 1927

4 Joslin, E P. Arteriosclerosis and Diabetes, *Ann Clin Med* **5** 1061 1927. Arteriosclerosis in Diabetes, *Ann Int Med* **4** 54, 1930

5 Allbutt, T C. Diseases of the Arteries, Including Angina Pectoris. London, Macmillan & Co, 1915, p 280

changes in diabetic children Morrison and Bogan⁶ found that the incidence of vascular calcification as determined by roentgenograms is higher in diabetic than in nondiabetic persons and that calcification increases with age and with the duration of diabetes Brown⁷ stated that every diabetic person over the age of 50 who has had diabetes for a few years will show arteriosclerosis of the feet on careful examination

On the other hand there are those who believe there is no direct relation between diabetes and vascular changes Hekimian and Vogel⁸ reviewing autopsies on 84 diabetic persons found no instance of death caused by arterial degenerative disease before the fourth decade 75 per cent died after the fifth decade Leutenegger⁹ investigating the clinical evidence of vascular change in 1 000 diabetic persons stated that a specific diabetic arteritis does not exist since positive evidence of such change was completely absent in those under 40 in about 50 per cent of his cases of five or more years standing there was no clinical evidence of vascular disease the latter occurring mainly in the sixth and seventh decades These and other writers have advanced the opinion that improvement in the treatment of diabetes has so lengthened the life span of diabetic persons that they now live long enough to acquire coincident nondiabetic degenerative arterial disease

In the clinic of sympathetic and vascular surgery of the Mount Zion Hospital, there is a considerable number of patients who complain of symptoms referable to disease of the peripheral arteries or who have been referred by other clinics because of subjective or objective evidence of abnormal peripheral circulation A number of these are diabetic persons in various advanced stages of degenerative arterial disease Impressed by the greater danger of such changes to diabetic than to nondiabetic persons we were led to examine clinically a series of 100 unselected patients with diabetes with a view to determining their status as to peripheral vascular disease In this investigation we sought not only the objective evidence of vascular disease but also the symptoms most commonly associated with disturbed peripheral circulation From the accumulated data we hoped to obtain information as to any existing relation between diabetes and peripheral arterial degenerative disease and as to any relation between the severity or duration of the diabetes and the extent of such arterial degeneration The data would furnish

6 Morrison L B and Bogan, I K Calcification of the Vessels in Diabetic Roentgenographic Study of Legs and Feet, *J A M A* **92** 1424 (April 27) 1929

7 Brown, A G Jr Diseases of the Blood Vessels of the Extremities in Diabetes *South Med & Surg* **92** 264 1930

8 Hekimian J and Vogel S A A Study of Diabetic Deaths Based on Autopsies, *New York State J Med* **34** 385 1934

9 Leutenegger F Klinisches Vorkommen von Gefäßveränderungen bei 1 000 Diabetikern *Ztschr f klin Med* **119** 165 1932

too, a baseline in accordance with which subsequent changes in the peripheral circulation could be more accurately gaged in future examinations

The patients were taken at random from the metabolic clinic. This clinic is under the direction of Dr. Russel Rypins, who has made a special study of diabetes. The diabetic patients are under close scientific surveillance. In addition, each patient rotates approximately every two months through a special chiropody clinic under the care of Dr. D. Kanter, who has been specially trained in the care of diabetic feet and who is well aware of the complications incident to ill advised chiropodic treatment for these patients. Frequent consultations are held between the physicians of these two clinics. With few exceptions the patients had not previously applied to the clinic of sympathetic and vascular surgery.

Our examinations consisted in the collection of certain important data from the history, including close questioning regarding symptoms of vascular disease. (This investigation of symptoms has been somewhat neglected in reports by others.) The patient was then put through a routine examination of the peripheral vascular system. Tables 4, 5 and 6 indicate the details of the history and the examinations used in determining the status of the peripheral circulation. The examination consisted not only in estimation of the strength of the peripheral pulses but especially in a clinical determination of the vascular sufficiency or insufficiency of the extremity as a whole. Roentgen studies were not routinely made because we are convinced that they are an unreliable index of the circulatory status. Patients not infrequently have advanced occlusive degenerative arterial disease, even of the arteriosclerotic type, without roentgenologically visible calcification, others, with widespread calcification, may have extremities with a well compensated peripheral circulation. Intradermal histamine tests were not routinely done because of the variability of the effect of histamine and because of the differences in interpretation to which the tests are subject. All examinations were done by members of the staff of the clinic of sympathetic and vascular surgery, who by reason of special training and experience were well qualified to estimate the desired factors. The observations made are presented in several tables, with accompanying explanations and comments.

INTERPRETATION OF TERMS AND SYMBOLS USED IN TABLES

Severity of Diabetes

Mild—Diabetes controlled by diet only

Moderate—Diabetes controlled by less than 15 units of insulin daily

Severe—Diabetes controlled by more than 15 units of insulin daily

Severity of Peripheral Vascular Symptoms

Mild—Mild pains cramps claudication, sensory disturbances, no incapacitation

Moderate—Considerable subjective complaints, distinct claudication, patient partially incapacitated

Severe—Severe symptoms ulceration gangrene amputations, marked claudication complete incapacitation

One or more of the foregoing symptoms determined the classification

Severity of Findings

Mild—Slight diminution of pulsation in one or two arteries, slight ischemia on elevation slight rubor on dependency

Moderate—Marked diminution of pulsation in more than one artery distinct elevation ischemia or dependent rubor healed ulceration, changes in color

Severe—Absence of pulsation in more than one artery very marked elevation ischemia or dependent rubor ulceration, gangrene, amputations

Arterial Pulsations

0—Absent

+-Barely perceptible

++—Distinctly perceptible but below normal

+++—Normally palpable

Ischemia on Elevation

or

Rubor on Dependency

0—Normal color

+-Slight

++—Distinct

+++—Very marked

Note that 87 per cent of the patients were over the age of 40 the greatest number being in the seventh decade. In patients under the age of 40 the incidence of severe diabetes was considerably higher than that of mild or moderate diabetes. Twenty-five per cent of the patients with severe diabetes 7 per cent of those with moderate diabetes and 6 per cent of those with mild diabetes were under 40.

The symptoms noted are those considered most important as indicating abnormalities of the peripheral vessels. They were compiled in accordance with a scheme which proved satisfactory in the clinic of sympathetic and vascular surgery. The high percentage of various sub-

jective disorders was striking. We found that 37 per cent of patients complained of pain, 31 per cent of cramps and 38 per cent of limitation of ability to walk. Twenty-six per cent were incapacitated by conditions

TABLE 1—*Distribution According to Severity of Diabetes*

Diabetes controlled by	No. of Cases		
	Mild	Moderate	Severe
Diet only	51		
Insulin, less than 15 units daily		14	
Insulin, more than 15 units daily			35

TABLE 2—*Distribution According to Sex*

Sex	Male	Female	
			37
			63
			100

TABLE 3—*Age Distribution in Relation to the Severity of Diabetes*

Severity of Diabetes	Age										Total No of Cases
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90		
Mild			1	2	12	10	18	7	1	51	
Moderate			1		1	7	3	2		14	
Severe		2	3	4	9	7	9	1		35	

TABLE 4—*Peripheral Vascular Symptoms and Their Relation to Severity of Diabetes*

Severity of Diabetes	Pain	Numbness	Burning	Other Sensory Disturbances	Cramps	Walking Ability (in Blocks)				Incapacitation Due to Arterial Disorg.	Color Changes	Inflammation	Ulcers	Varicose Veins	Gangrene	Amputations	Reaction to Heat and Cold	Total Number of Cases
						Less than 1	1-2	Up to 5	Up to 10	More than 10								
Mild	17	17	6	11	19	2	1	10	8	30	11	3	2	7	20	3	1	8
Moderate	7	5	3	5	4	1		4	2	7	6	2	4	2	6	2	1	14
Severe	13	8	5	5	8	2	3	3	2	25	9	2	2	4	5	12	2	35

originating in the peripheral vascular system. We were surprised to find such a high incidence of decreased ability to walk in patients taken at random who did not consult the clinic. Pain was present in 30 per cent of 51 patients with mild diabetes and 50 per cent of 14 with moderate diabetes but in only 37 per cent of 35 with severe diabetes. Limitation of ability to walk occurred in 41 per cent of patients with mild diabetes

43 per cent of patients with moderate diabetes and 26 per cent of patients with severe diabetes. These figures show the absence of any direct relation between the presence of symptoms and the severity of diabetes.

Of 197 lower extremities the dorsalis pedis pulse was diminished in 50 (25 per cent) and not perceptible in 21 (10.5 per cent) a total of 35.5 per cent of abnormal dorsalis pedis pulses. This pulse was impalpable in 10 per cent of the extremities of persons with mild diabetes, 18 per cent of the extremities of persons with moderate diabetes and only 9 per cent of the extremities of persons with severe diabetes. This again shows the absence of any direct relation between the severity of the diabetes and the palpability of the dorsalis pedis pulse. The high incidence of decreased dorsalis pedis pulsation is noteworthy even among

TABLE 5—*Pulsation of the Peripheral Arteries of the Extremities*

Severity of Diabetes	A dorsalis pedis (197 pulses)								A tibialis posterior (197 pulse)							
	0		+		++		+++		0		+		++		+++	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Mild	4	6	7	5	12	13	27	27	5	10	10	9	10	12	22	19
	1*	1*							1*	1*						
Moderate	3	2	2	2		2	9	8	3	4	3	2	3	3	5	5
Severe	3	3	1		3	5	27	28	5	6	3	5	6	5	20	21
	1*								1*							
Severity of Diabetes	A poplitea (168 pulses)								A femoralis (200 pulses)							
	0		+		++		+++		0		+		++		+++	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Mild	2	2	1	3	9	9	39	37	1	1			2	3	48	47
Moderate	1*			1		5	8	10					1	1	13	13
Severe	1*				7	8	27	27					4	2	31	33

* Pulse missing (amputation)

patients with mild diabetes. Abnormal dorsalis pedis pulsations are rare in normal persons.

The incidence of insufficient pulsations is still higher in the posterior tibial artery where only 92 of 197 extremities showed normal pulsations. Complete absence of pulsation was noted in 18 per cent of the extremities of persons with mild diabetes, in 25 per cent of those with moderate diabetes and in 16 per cent of those with severe diabetes. Similar relations were found in the popliteal artery where 50 abnormal pulsations were found and in the femoral artery where only 15 were abnormal. It is thus clearly evident that whereas the diminution of peripheral pulsations is a common finding in unselected cases of diabetes, one can make no conclusions from the severity of the diabetes regarding the extent of changes in the peripheral pulses.

Table 6 shows the more important observations indicating the circulatory status. The degree of "elevation ischemia" and "dependent rubor" are fully given, since we consider these conditions of special value in determination of the general vascular competency of the extremity. Abnormal rubor on dependency was found in 51 per cent of mildly diabetic, 68.5 per cent of moderately diabetic, and 28.5 per cent of severely diabetic persons, abnormal ischemia on elevation was found in 34 per cent of mildly diabetic, 21.4 per cent of moderately diabetic and 7.1 per cent of severely diabetic persons. Thus again we see a relatively high percentage of vascular insufficiency in patients with mild

TABLE 6—*Peripheral Circulatory Observations in Relation to Severity of Diabetes*

Severity of Diabetes	Rubor on Dependency						Ischemia on Elevation						Sudden Changes in Temperature					
	0		+		++		+++		0		+		++		+++			
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Mild	24	11	10	9	10	6	6	34	5	5	10	9	2	3	19	20		
Moderate	3	1	2	7	7	1	1	10	2	2			1	1	3	3		
Severe	23		3	7	5	1	2	30	2	1	1	1			7	7		

Severity of Diabetes	Trophic Disturbances		Color Changes		Gangrene		Ulcerations		Varicose Veins		Sensory Disturbances		Amputations		Sclerosis of Vessels	Total Number of Cases
	R	L	R	L	R	L	R	L	R	L	R	L	R	L		
Mild	1		1	3			1	1	18	19		1	1	1	26	51
Moderate	1				1		1		6	5	2	1		1	4	14
Severe	3	3					1		6	6			2		8	30

TABLE 7—*Associated Diseases in Relation to the Severity of Diabetes*

Severity of Diabetes	Total No of Cases	Generalized Arteriosclerosis	Arterial Hypertension	Angina Pectoris
Mild	51	31	31	7
Moderate	14	5	5	2
Severe	35	14	13	2

diabetes and the highest degree in those with moderate diabetes while those with severe diabetes have the lowest incidence.

Table 7 indicates the incidence of disorders of the general vascular system and their frequency in the various degrees of diabetes. There is nothing to indicate that the frequency of these disorders increases with the severity of diabetes. In fact, the highest percentage was found among the patients with mild diabetes.

It is interesting that 8 (59 per cent) of 14 patients with diabetes of less than one year's standing had definite generalized arteriosclerosis. Not one of the patients with arteriosclerosis was under the age of 51. Irrespective of age, 52 per cent of patients with diabetes of five years'

duration or less showed generalized arteriosclerosis whereas 70 per cent of those with disease of over five years' duration displayed generalized arteriosclerosis

TABLE 8—*Presence of Arteriosclerosis in Relation to Duration of Diabetes*

Duration of Diabetes	Arteriosclerosis											Number of Arterio- sclerotic Patients	Num- ber of Cases
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100			
Less than 1 year						2	6				8	14	
1 year							1				1	2	
1-2 years					1	3		1			5	7	
2-3 years							1				1	9	
3-5 years					1	3	4	3			11	18	
5-10 years						2	6	5			13	23	
10-15 years						1	4	1			6	9	
15-20 years							2				2	6	
20-30 years										1	1	5	
More than 30 years												1	

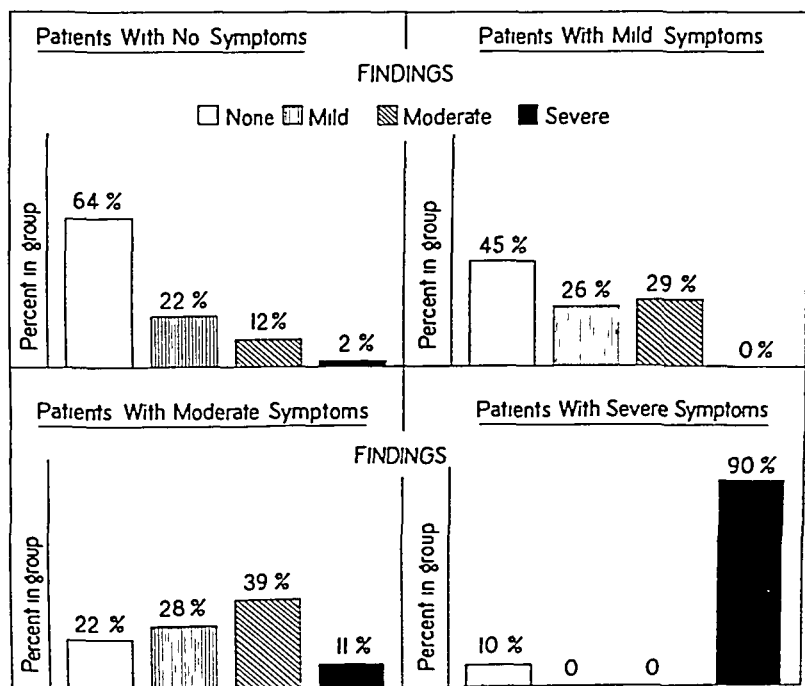


Chart 1—Symptoms and findings in cases of mild, moderate and severe diabetes

Although the foregoing tables show no definite relation between the degree of symptoms or of findings and the severity of the diabetes, there is a direct relation between the degree of symptoms and the objec-

tive findings In 64 per cent of cases in which there were no symptoms there were no objective findings, whereas in 90 per cent of those with severe symptoms there were marked findings Data on patients with mild and moderate symptoms may be noted in the chart Thus the search for symptoms of peripheral vascular disorder, often neglected by other authors, gives a valuable clue to the presence of objective vascular abnormalities

TABLE 9—*Relation of Duration of Diabetes to Severity of Symptoms*

Duration of Diabetes	Symptoms				Total Number of Cases
	None	Mild	Moderate	Severe	
Less than 1 year	9	1	4		14
1 year	1	1			2
1 2 years	3	3		1	7
2 3 years	5	2	2		9
3 5 years	4	9	3	2	18
5 10 years	12	10	4	3	29
10 15 years	4	2	1	2	9
15 20 years	3	1	1	1	6
20 30 years		2	2	1	5
More than 30 years			1		1

TABLE 10—*Relation of Duration of Diabetes to Severity of Findings*

Duration of Diabetes	Findings				Total Number of Cases
	None	Mild	Moderate	Severe	
Less than 1 year	7	4	3		14
1 year	2				2
1 2 years	4	2	1		7
1 2 years	4	3	1		9
2 3 years	5	3	1	4	18
3 5 years	10	3	1		20
3 5 years	12	7	6	4	29
5 10 years	2	1	4	2	9
10 15 years	3		2	1	6
15 20 years		2	2	1	5
20 30 years			1		1
More than 30 years					

Whereas all symptoms and findings are more frequent in cases of diabetes of long standing, there are a goodly number of persons with diabetes of long standing who have no symptoms or findings Again, we may note that findings were absent in 50 per cent of persons with diabetes of less than one year's standing and also in 50 per cent of those with diabetes of from fifteen to twenty years' standing The relation of the duration of the diabetes to the severity of symptoms is comparable Thus it cannot be concluded that the duration of diabetes has any relation to the severity of the peripheral vascular symptoms or findings

Charts 2 and 3 show that in the greatest number of cases in which there were symptoms and findings of peripheral arterial disease the patients were in the age groups in which peripheral arterial disease occurs most frequently in nondiabetic persons. There were no patients with severe symptoms or severe findings below the sixth decade.

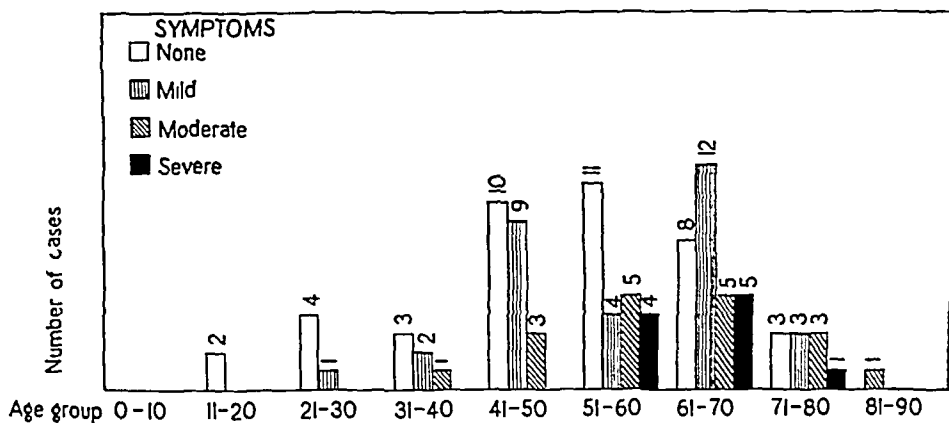


Chart 2—Severity of symptoms correlated with age

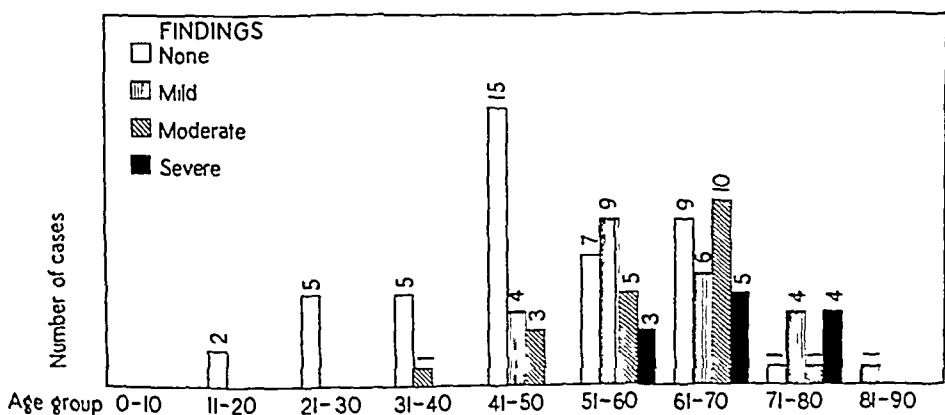


Chart 3—Severity of findings correlated with age

SUMMARY

One hundred diabetic persons, selected at random were examined to determine the presence of symptoms and objective findings of peripheral arterial disease.

Over half of the patients complained of vascular symptoms. The majority showed abnormalities in the peripheral pulses and other signs of peripheral vascular derangement.

Generalized arteriosclerosis was present in 50 per cent. The greatest number of these patients were mildly diabetic persons in the older age group. The incidence of generalized arteriosclerosis showed no relation to the duration of the diabetes.

Generalized arteriosclerosis did not occur in any diabetic patient under the age of 40 and occurred in only 2 of the patients in the fifth decade.

There was no relation between the duration of diabetes and the severity of either the symptoms or findings of peripheral arterial disease.

There is a direct relation between the severity of symptoms and the severity of findings of peripheral arterial disease. The search for symptoms is important as an indication of the presence of objective evidence of peripheral arterial disease.

Findings of peripheral vascular origin were most prevalent in the age groups in which degenerative arterial disease occurs most frequently in nondiabetic persons.

CONCENTRATION OF PROCAINE IN THE CEREBRO- SPINAL FLUID OF THE HUMAN BEING AFTER SUBARACHNOID INJECTION

SECOND REPORT

H KOSTER, M D

A SHAPIRO, M D

AND

R WARSHAW, B A

BROOKLYN, N Y

In previous communications¹ we presented data on the concentration of procaine at three levels in the cerebrospinal fluid of 122 adult patients at various times after the subarachnoid injection of 150 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid.

To obtain more information regarding the factors which influence the distribution of the anesthetic in the subarachnoid space we investigated the effect of varying (1) the dose, (2) the volume and (3) the dose and the volume in the same proportion.

METHOD

Adult patients each received an injection of procaine hydrochloride, dissolved in cerebrospinal fluid, into the subarachnoid space at the interspace between the second and the third lumbar vertebra and were immediately placed in the Trendelenburg position (5 to 8 degrees).

The patients in group B received 300 mg of procaine hydrochloride dissolved in 3.5 cc of cerebrospinal fluid and those in group C received 300 mg of procaine hydrochloride dissolved in 7 cc of cerebrospinal fluid. Samples of cerebrospinal fluid were withdrawn at different times after injection as follows:

- Group B From 85 patients, 1 cc at the site of injection (chart 1)
 From 47 patients, 1 cc three interspaces above the site of injection (chart 2)
 From 24 patients, 2 cc at the cisterna magna (chart 3)
- Group C From 65 patients, 1 cc at the site of injection (chart 4)
 From 53 patients, 1 cc three interspaces above the site of injection (chart 5)
 From 25 patients, 2 cc at the cisterna magna (chart 6)

From the Crown Heights Hospital

1 Koster, H, Shapiro, A, and Leikensohn, A. (a) Spinal Anesthesia: Procaine Concentration Changes at the Site of Injection in Subarachnoid Anesthesia. *Am J Surg* **33** 245-248 (Aug) 1936. (b) Concentration of Procaine in the Cerebrospinal Fluid of the Human Being After Subarachnoid Injection. *Arch Surg* **37** 603-608 (Oct) 1938.

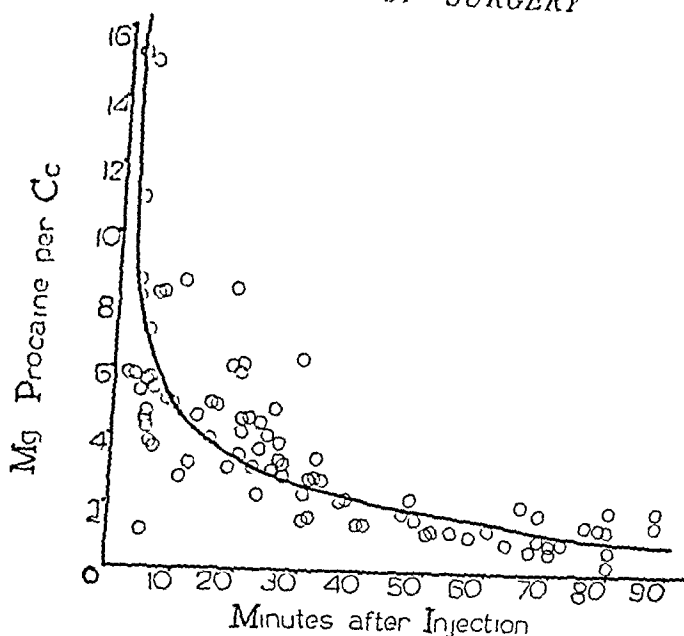


Chart 1—Concentration of procaine in the cerebrospinal fluid at the site of injection of 300 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid

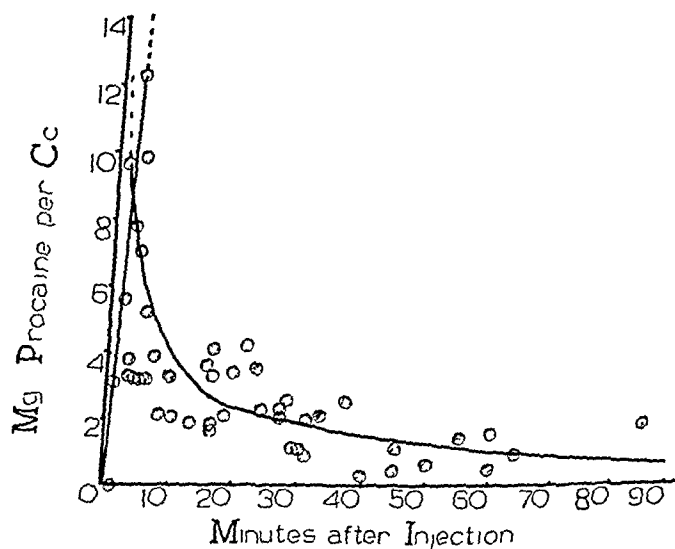


Chart 2—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of 300 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid

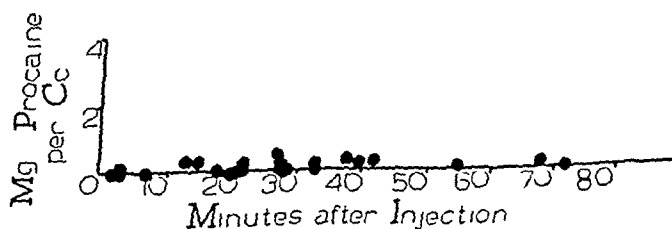


Chart 3—Cisternal concentration of procaine in the cerebrospinal fluid after injection of 300 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid

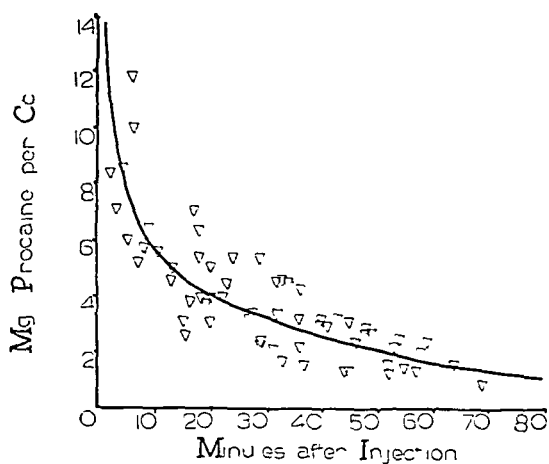


Chart 4—Concentration of procaine in the cerebrospinal fluid at the site of injection of 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid

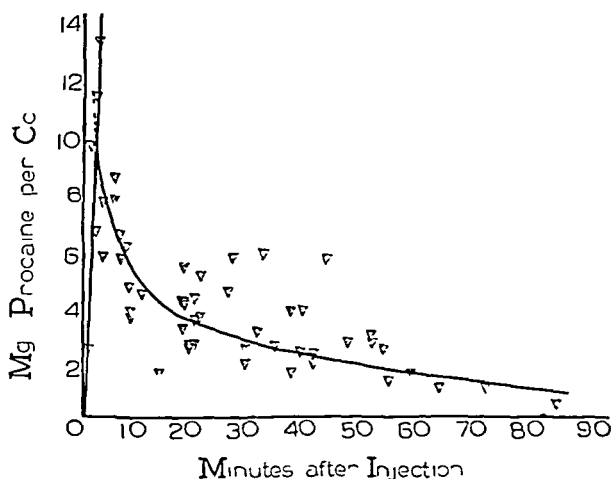


Chart 5—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid

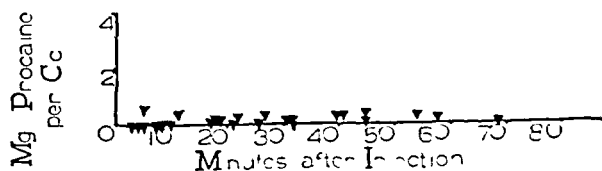


Chart 6—Cisternal concentration of procaine in the cerebrospinal fluid after injection of 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid

The concentration of procaine hydrochloride in these samples was determined in duplicate by the micromethod previously described.² The results are shown graphically (charts 1 to 6). Each point represents an average of duplicate.

The curves in chart 7 represent the concentration of procaine at the site of injection. It is seen that the curves are approximately the same shape. The ordinates of curve A (150 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid) are approximately one-half the values of those of curve B (300 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid). The ordinates of curve C (300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid) are similar to those of curve B but slightly above them.

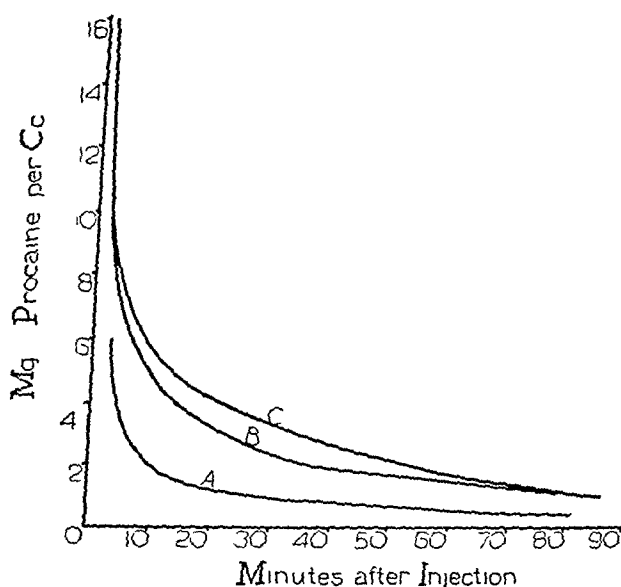


Chart 7—Concentration of procaine in the cerebrospinal fluid at the site of injection of (A) 150 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid, (B) 300 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid and (C) 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid.

The curves in chart 8 represent the concentration of procaine three interspaces above the site of injection. Here again the curves are approximately the same shape and have the same relation to each other as do the corresponding curves in chart 7.

The concentrations at the cisterna magna for 300 mg are approximately twice the value of those obtained with 150 mg (reported elsewhere^{1b}), and the percentage of samples giving negative results is smaller.

² Koster, H., Shapiro, A., and Posen, E. A Method for the Microdetermination of Procaine in the Cerebrospinal Fluid, *J Lab & Clin Med* 21: 1096-1100 (July) 1936.

COMMENT

The fact that the concentration of procaine in the cerebrospinal fluid is approximately doubled when a double dose of procaine hydrochloride is injected suggests the possibility that mechanical rather than chemical factors are largely responsible for the phenomena observed. It is surprising, however, that the concentration changes so little when a double volume of cerebrospinal fluid is used to dissolve the injected anesthetic. It might be expected that the injection of 300 mg of procaine hydrochloride dissolved in 7 cc of cerebrospinal fluid would give concentrations lower than those following the injection of 300 mg of procaine hydrochloride dissolved in 35 cc of cerebrospinal fluid.

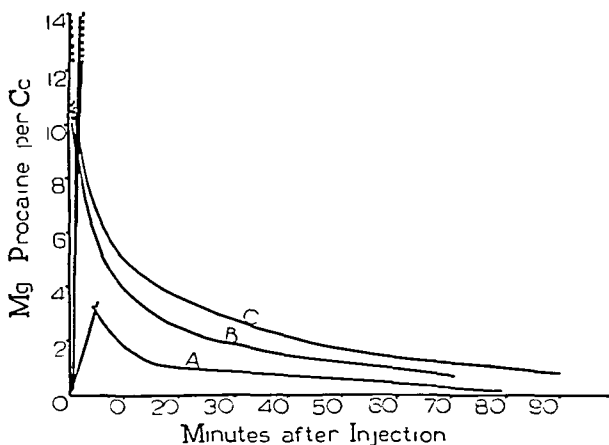


Chart 8—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of (A) 150 mg of procaine hydrochloride in 35 cc of cerebrospinal fluid, (B) 300 mg of procaine hydrochloride in 35 cc of cerebrospinal fluid and (C) 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid

Our observations show a slight and probably insignificant difference in the opposite direction.

It is of interest to compare the maximum values found at different levels in single cases during the course of anesthesia (chart 9). These represent extreme values found in single cases and are not composite results. At the site of injection the maximum concentration is the initial concentration and depends on the concentration of the injected solution. Three interspaces above the highest concentration with all three types of injection was found after three minutes (chart 9) and was approximately three times as great after the 300 mg injections as after the 150 mg injection (4 mg, 12.3 mg and 13.2 mg per cubic

centimeter) At the cisterna magna the maximum concentration with the 300 mg doses were also approximately three times that with 150 mg (0.6 mg, 0.5 mg and 0.2 mg per cubic centimeter) Both in the composite curves and in the extreme values the great fall of concentration in the cephalad direction confirms our previous conclusion that the Trendelenburg posture does not cause concentrated solutions of procaine hydrochloride to flow down to the cisterna as do colored solutions in manimate models

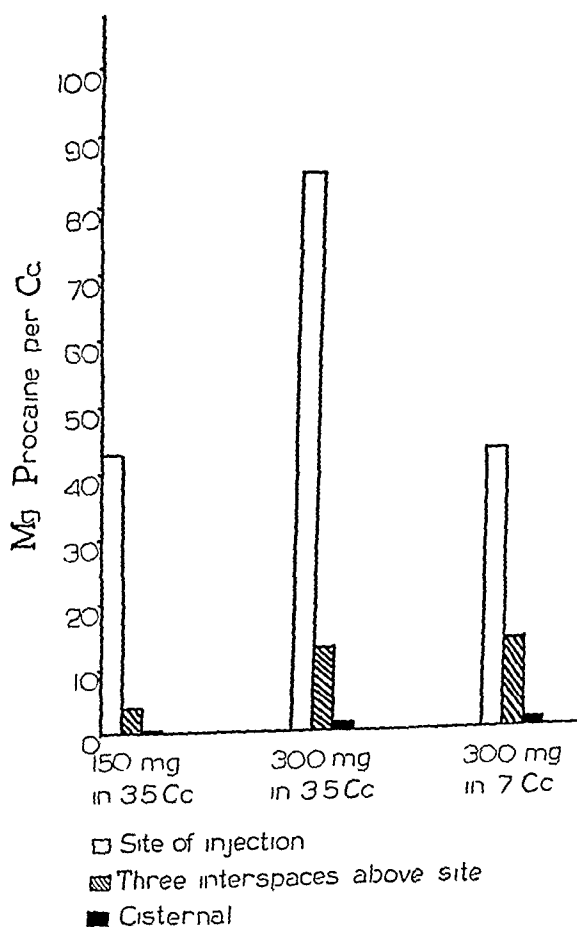


Chart 9—Maximum concentrations of procaine in the cerebrospinal fluid

CONCLUSIONS

The concentrations of procaine at the site of injection, three interspaces above the site of injection and at the cisterna when after injection of 300 mg of procaine hydrochloride in 35 cc of cerebrospinal fluid and 300 mg of procaine hydrochloride in 7 cc of cerebrospinal fluid parallel the findings previously described as occurring after the injection of 150 mg of the anesthetic dissolved in 35 cc of cerebrospinal fluid

The injected procaine hydrochloride spreads rapidly away from the site of injection in a cephalad direction, so that the concentration of

procaine falls there and rises in the dorsal region. At no time does the concentration in the dorsal region reach as high a level as that found simultaneously in the lumbar region. When the concentration at the dorsal level has reached its maximum, it decreases at approximately the same rate as at the lumbar level and presumably for the same reasons.

Since the patients were in the Trendelenburg position from the time of injection to the time of sampling, our data do not support the assumption that the Trendelenburg position causes concentrated solutions of procaine hydrochloride to flow down to the cisterna as do colored fluids in glass models.

Doubling the amount of procaine hydrochloride injected approximately doubles the concentration found in the cerebrospinal fluid.

Doubling the volume of the injected solution causes no significant change.

MIGRAINE CAUSED BY DEMONSTRABLE PATHOLOGIC CONDITIONS

REPORT OF A CASE WITH CURE BY REMOVAL OF SMALL TUMOR
IN CALCARINE FISSURE

OLAN R. HYNDMAN, M.D.
IOWA CITY

Whatever may be the cause of migraine, I believe the consensus is that its mechanism resides in the cerebrum and probably in the cortical vessels. The almost consistent association of the headache with fortification figures, the occurrence of which usually is the prodromal or initial event in an attack, strongly suggests that the mechanism has its beginning about the calcarine fissure.

So far as I can ascertain, no pathologic condition of the visual cortex or other structures in the brain has been found which could unequivocally be pointed out as the exciting factor in migraine. Because I feel that such a condition can be demonstrated in the case to be described I am presenting the following report.

REPORT OF CASE

L. I.,¹ a white woman aged 30, was referred to me by Dr. C. M. Wray, of Iowa Falls, Iowa, in October 1936.

Chief Complaint—The patient complained of headache and light flashes.

Present Illness—Six years previously she had had her first attack of migraine. The pain was generalized in the head and was severe and throbbing. It lasted twenty-four hours and was associated with nausea and vomiting. The attack was not accompanied by flashes of light or other noticeable phenomena. After this she had frequent light attacks of headache, but one year later she had a second severe attack. The ache was referred largely to the top of the head and was made worse and more throbbing when she stooped. This attack also lasted twenty-four hours. Thereafter she suffered a hard attack associated with nausea and vomiting at least once each month, with lighter attacks in the intervals, except during a period of four months before and three months after a delivery.

She attributed the headaches to nervousness and fatigue. One year before admission to the hospital, after a hard day's work, she had had "cold and hot

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1 The case of this patient was reported from a ventriculographic standpoint in the following paper: Hyndman, O. R. Cerebral Pneumography. Ventriculographic Interpretation of Tumors In and About Third Ventricle, Aqueduct of Sylvius and Fourth Ventricle, Arch Surg 36:245-291 (Feb.) 1938.

spells" Headache was developing, for which she retired at 4 p. m. The next morning she "awoke in the hospital." At 6 p. m. her sister-in-law had found her talking irrationally, with a high fever (). She was discharged from the hospital in twenty-four hours. She walked home, although her head was aching severely. The next day she was well, and she remained so until the delivery of a child, four months later.

Three months after the delivery the severe headaches associated with nausea and vomiting began again and occurred at intervals of two weeks to a month until the time of admission. They came on at any time during the day or night. At times she would retire feeling well and be awakened by a severe attack.

Ordinary methods of treatment, including rest and cold applications, were of no avail. Only hypodermic injections of morphine gave any relief.

About one month before her admission to the hospital she had a seizure or varicolored light flashes in the left visual field "as if some one were waving red and green lanterns over her left shoulder." These seizures lasted from two to four minutes and at times recurred at half-hour intervals. During the seizures

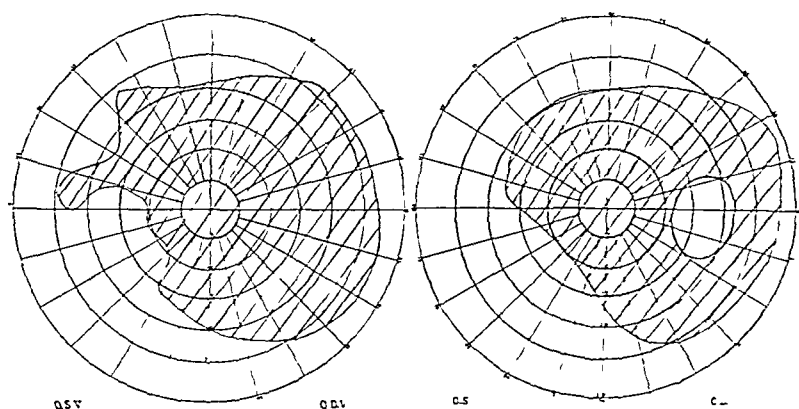


Fig. 1—Visual fields, showing a defect in the left homonymous fields

there were transitory weakness of the left arm and leg and lack of control of these extremities. Her husband stated that at such times she handled her left leg like a high-stepping horse.

She stated that there was no association between the headaches and the visual phenomena.

The family history was relevant only in the fact that none of the patient's relatives had been subject to migraine or had had any condition similar to her present illness.

Examination.—General examination gave essentially negative results. The patient was obese and cheerful. The temperature was 98.2 F, the pulse rate 88 and the blood pressure 110 systolic and 70 diastolic.

Neurologic study, including examination of the ocular fundi, gave essentially negative results except for evidence of left homonymous hemianopia by gross tests. The visual fields are shown in figure 1.

Laboratory Examination.—Studies of the urine and of the blood revealed normal conditions. The Wassermann reaction was negative. The spinal fluid pressure was within normal limits.

Röntgen Examination—A plain roentgenogram of the skull revealed a small diffuse area of calcification in the left parietal region. It was about 1 cm from the skull and measured about 1.5 cm in diameter.

Ventriculographic Examination—A ventriculogram was made and proved to be normal in every respect.

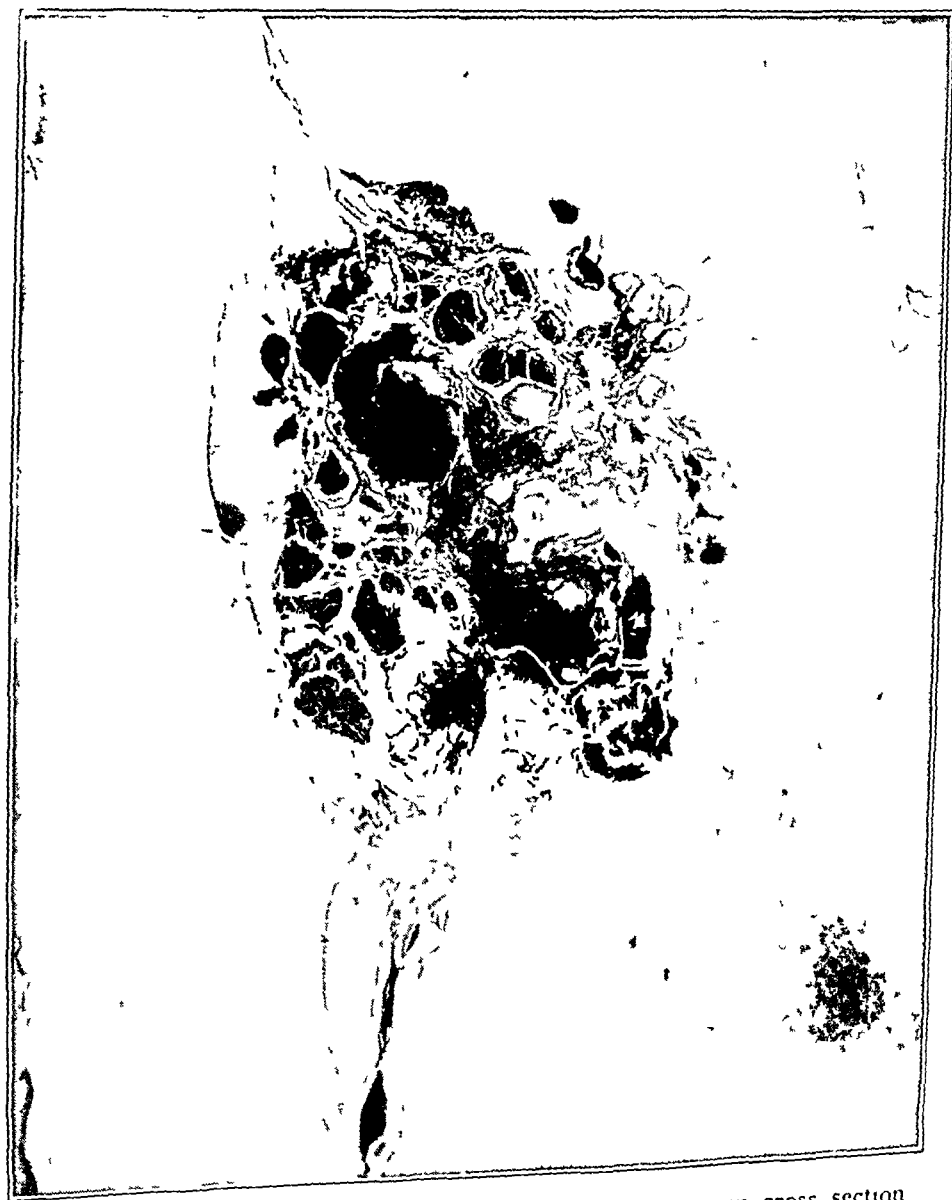


Fig. 2—Low power photomicrograph showing the tumor in cross section.

Operation—On October 6 the right occipital lobe was explored. The cortex of the brain appeared normal in every respect. There were none of the signs of increased intracranial pressure. The occipital lobe was inspected mesially, but nothing unusual could be seen. In view of the history and visual fields, however, amputation of the right occipital pole, including the calcarine fissure, was felt to be justified. The plane of excision was made about $1\frac{1}{2}$ inches (3.7 cm) anterior to the posterior tip of the occipital pole.

Pathologic Observations—On examination of the specimen a tumor about 1 cm in diameter could be seen directly embedded in the region of the calcarine fissure (This growth is shown in figure 7 of the previous report¹) Microscopically the tumor proved to be a hemangioma, with evidence of recent and old hemorrhage (fig 2)

Course—The patient recovered, and to the time of writing (two years) she has been free from headache, light flashes and seizures of transient weakness in the left arm and leg

COMMENT

Although it might be questioned that this patient presented a typical migraine syndrome, she nevertheless presented the major elements of that syndrome. The important feature of the case is the fact that there were frequent seizures of severe migrainous headache associated with nausea and vomiting and relieved only by morphine but responding promptly to removal of the pathologic tissue. So far as is known, the patient at no time had increased intracranial pressure and the ventriculogram was normal in every respect. It seems clear that the lesion removed was the factor responsible for the headaches. The tumor itself was in the region of the right calcarine fissure and did not involve the dura. It seems fair to assume, therefore, that this is a case of an organic lesion causing attacks of migrainous headache through the same mechanism that is responsible for "idiopathic migraine" and that it provides additional evidence that this mechanism operates within the limits of the cerebrum, including its vessels and the leptomeninges.

OSSEOUS CHANGES ASSOCIATED WITH LYMPHO-GRANULOMA VENEREUM

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Reports of cases in which articular changes are associated with lymphogranuloma are infrequent, and reports of the association of osseous lesions with this condition are rare. Many writers have mentioned arthritic symptoms as one of the early acute manifestations of the disease. Frei¹ stated that "rheumatoid symptoms, sometimes with joint swelling" are present, and he offered the fact as evidence of the constitutional nature of the malady. Hellerstrom² noted polyarthritic symptoms in 3 of his cases. A complete report was made by Reichle and Connor³ of a case in which there was involvement of the hip joint, this is the only report of such involvement we were able to find in the American literature. We have been impressed by the paucity of detailed case reports describing osseous and articular changes associated with lymphogranuloma and also by the fact that the data revealed by study of the records seemed to be incomplete and inadequate for critical scientific appraisal. It seemed, therefore, important to review the literature and to report 3 personally observed cases of osseous changes occurring late in the disease.

REVIEW OF LITERATURE

Koppel,⁴ in 1927, reported the case of a 28 year old woman who was admitted to the hospital because of a painful swelling in the right inguinal region. The right inguinal lymph nodes were fluctuant. The right wrist and the left ankle joint were swollen. The left wrist and the right

From the Surgical Service of the Harlem Hospital, Louis T Wright, Director

1 Frei, W. Venereal Lymphogranuloma, *J A M A* **110** 1653 (May 14) 1938

2 Hellerstrom, S. A Contribution to the Knowledge of Lymphogranuloma Inguinale, *Acta dermat-venereol*, 1929, supp 1, p 5, cited by Allen, R C. Rectal Stricture. Relation to Lymphopathia Venerea. *Tr Am Proct Soc* **35** 150 1934

3 Reichle, H S, and Connor, W H. Lymphogranuloma Inguinale. Report of a Case with Involvement of the Retroperitoneal Lymph Nodes and Probable Involvement of the Hip Joint, Adrenals and Kidneys, with Autopsy, *Arch Dermat & Syph* **32** 196 (Aug) 1935

4 Koppel, A. Lymphogranuloma Inguinale, mit akuten rheumatischen Erscheinungen, *Klin Wchnschr* **6** 2469 1927

ankle swelled later Erythema nodosum then developed, with lesions on both legs and elsewhere on the body The history included syphilitic infection, five courses of antisyphilitic treatments had been given At the time of admission both the Wassermann and the Frei reaction were positive The patient had fever during her two weeks' stay in the hospital, but before her discharge the erythema nodosum and the articular symptoms had disappeared and the temperature had become normal No roentgen studies were made, and serologic data were not reported

Frauchiger⁵ reported 2 cases The patient in the first was a 48 year old woman who entered the hospital in 1933, complaining of stiffness of the right ankle, swelling of the left ankle and pain and swelling in both hands In 1916 her husband had had a urethral discharge, swelling of the inguinal lymph nodes on the right, and pain in the right hip Later in the same year the patient had had an ectopic pregnancy and a Bartholin abscess In 1918 she had pain in both ankles In 1923 she had a rectal discharge and in 1928 a rectal abscess Rectal stenosis followed the abscess, and a colostomy was performed Physical examination on admission showed thickened tender elbow joints, with limitation of articular motion The left ankle was swollen, but there was no pain on motion Roentgen examination of the chest and Mantoux tests gave negative results Roentgen examination of the joints showed porotic changes and atrophy from disuse of the knee joints which were thickened and contained fluid There was thickening of the lateral sides of the capitellum radii, with thickening of the lateral portion of the joint capsules and periostitis of the lateral surface of the radiuses

Frauchiger's second case was that of a 33 year old man who entered the hospital in 1933 complaining of pain in the right wrist joint He stated that he had practiced sodomy in 1924 and that this practice was followed by abscesses of the inguinal glands His Wassermann reaction was positive at that time, and he was given antisyphilitic therapy Rectal stenosis developed Later he was operated on for a hernia and subsequent to this a colostomy was performed After the colostomy there was severe pain in the back and pain and swelling were observed in both ankle joints In 1933 motion of the right wrist caused pain and the wrist was somewhat stiff There was swelling on the volar surface The Frei reaction was positive Results of Wassermann tests and complement fixation tests for gonorrhea were doubtful A few days later a para-articular abscess developed and was incised The pus was greenish yellow and odorless It contained leukocytes but no bacteria Injection of this pus into laboratory animals showed no tubercle bacilli No mention was made of roentgen study

⁵ Frauchiger E Polyarthrit. lymphogranulosa inguinalis Arch. Schweiz. med. Wchnschr. 63: 1207 1933

Reichle and Connor reported the case of a 31 year old Negro first seen in January 1932. He complained of pain in the right groin, which interfered with walking and became severe on extension of the thigh. Two months previously he had had a urethral discharge for fifteen days. Three weeks later he had noticed swelling in the right inguinal region, followed by spontaneous rupture of the mass and discharge of a large amount of pus. The right inguinal glands were enlarged on admission. The Frei reaction was positive. The Wassermann reaction varied from negative to 3 plus on different occasions. The patient was given seventeen intravenous doses of typhoid vaccine, which was administered bi-weekly. After this he received four intravenous injections of 1 per cent antimony and potassium tartarate. Suppuration of the nodes continued. On March 17 complete resection of the right inguinal nodes was done. Postoperatively the temperature varied between 98.6 and 104 F. Pain in the right hip continued, but a roentgenogram of the joint at this time was normal. The upper end of the surgical wound was infected and discharged pus. A roentgenogram of the hip joint one month later showed a destructive process. Arthrotomy performed on April 23 released pus from the joint and revealed eroded articular cartilage. The wound was drained, and the leg was fixed in extension. The patient died on May 20. At autopsy the right hip joint contained a small amount of dark fluid, and the articular surfaces of the acetabulum and the head of the femur were roughened and discolored. The sinus observed in the right inguinal region extended into the right hip joint. The lymphatic chain from the inguinal region extended along the retroperitoneal nodes to the diaphragm, and the nodes showed the typical lesions of lymphogranuloma. This case was more thoroughly studied than any of the other cases in the literature.

Carrasco⁶ examined a 22 year old man in December 1934 for bilateral enlargement of the inguinal nodes. Antisyphilitic treatment had been given, and the Wassermann reaction was negative. On two occasions the Frei test gave a markedly positive reaction, progressing even to necrosis. There was pain in the right hip joint, and extension of the leg was painful. A fresh mass of enlarged glands developed in the right iliac fossa. After about ten days the arthritis disappeared and the patient returned to work. No roentgen examination was reported. Carrasco's second case was that of a 24 year old man seen in January 1935. There was bilateral enlargement of the inguinal nodes, with marked adenopathy in the right iliac fossa and pains in the right leg. The Frei test gave a markedly positive result on two occasions. In March 1935 the patient was obliged to stay in bed because of sharp

⁶ Carrasco, C. *Maladie de Nicolas-Favre avec arthrite de la hanche*. Bull Soc. franç. de dermat. et syph. **43** 1556, 1936.

pains in the right hip. Two weeks later the arthritis disappeared. No roentgen studies were reported.

Sezary and Saliembiez⁷ reported 1 case. They examined a 31 year old woman who complained of pain in the knee joint in March 1936. She had had syphilis in 1932, Bartholinitis in 1933 and an inguinal bubo resembling lymphogranuloma venereum in 1933. The inguinal bubo did not heal until April 1934. The Frei test at this time gave a positive result. A rectal stricture developed in January 1934. An iliac anus was created in October 1934. There had been two previous attacks of hydrarthrosis, in November 1934 and April 1935. Fluid withdrawn from the knee in March 1936 was injected into three different kinds of laboratory animals, but the results were not illuminating. A Frei antigen made from the fluid produced a positive intradermal reaction in the patient and in other patients known to be suffering from lymphogranuloma venereum but the patient's serum had no such power. Injections of anthiomaline (the lithium salt of stibiothiomalic acid) were credited with curing the hydrarthrosis. No roentgen studies were reported.

Midana⁸ reported the case of a 34 year old man who complained of pain in the right coxa-femur joint and enlarged nodes in the right inguinal region. An enlarged inguinal node had developed three months previously, but its incision had caused only temporary relief. Examination showed enlargement of the deep iliac glands. A diagnosis of inguinal paradenitis was made and was confirmed by the Frei test. Roentgen study showed no osseous lesions in the head of the femur or the acetabular bones, but the articular 'interlinea' was 'opacified'. Midana stated that treatment with antimonial preparations cured (clinically) the adenopathy and the articular lesions in a little over three weeks.

Summary of the Literature—Koppel's patient had both syphilis and lymphogranuloma. The differential diagnosis in this case was incomplete. This, with the absence of roentgen studies, makes us classify it as a case in which the picture was only suggestive of osseous changes. In Frauchiger's first case definite osseous changes were seen on roentgen examination. His second case was one of syphilis and lymphogranuloma, with tuberculosis ruled out. His failure to rule out gonorrhea and to make roentgen studies makes it unacceptable. In the case reported by Reichle and Connor although syphilis was associated with lymphogranuloma, the articular changes found were so closely related to the suppurating inguinal glands (which did not respond to thorough

7 Sezary, A., and Saliembiez, M. Hydrarthrose récidivante et maladie de Nicolas-Favre, *Bull. Soc. franç. de dermat. et syph.* **43**: 1573, 1936.

8 Midana, A. Artrite dell' anca di origine porodentica. *Mirerra med.* **1**: 434, 1937.

antisyphilitic treatment) that in the light of our present knowledge we believe the articular lesion to have been due to lymphogranuloma. In Carrasco's 2 cases, which were instances of lymphogranuloma, the diagnosis of arthritis was based simply on pain in the joints. Because of lack of roentgen examination and insufficient data, the diagnosis must be considered presumptive. The case reported by S  zary and Salembiez proved to be one of hydatidosis in a woman with syphilis, gonorrhea and lymphogranuloma. The reactions obtained with the joint fluid antigen adds weight to the evidence that the pathologic condition of the joints was due to the lymphogranuloma virus. In Midana's case slight changes were observed in roentgen examination, but we doubt that any serious bone lesion would heal so rapidly.

Since there are so few proved cases of osseous and articular lesions reported in the literature, it seems desirable to outline certain minimal standard requirements that should be fulfilled before a diagnosis is made. We suggest the following diagnostic criteria:

- 1 The clinical symptoms should be those of lymphogranuloma venereum.
- 2 The Frei reaction should be positive.
- 3 Pathologic, bacteriologic, serologic and roentgen studies must rule out tuberculosis, syphilis, gonorrhea, malignant tumors and pyogenic infections.
- 4 Definite changes in bones or joints should be evident roentgenographically.

It is only by the use of such rigid standards that one is able to differentiate many cases in which there are signs and symptoms simulating osseous or articular changes due to lymphogranuloma from the few cases in which the manifestations are undeniably due to this disease.

It should be pointed out again how rarely pathologic conditions of the bones occurring in the late stages of this condition are encountered. Hartmann,⁹ of Paris, in a painstaking and intensive study of rectal stenosis over a period of forty years, has not recorded in any of his many carefully detailed case histories a single instance of involvement of the bones. In a further study of this point we have examined roentgenographically 25 patients with rectal strictures with positive Frei tests. The pelvis, hip joints and lumbar vertebrae were found to be normal.

REPORT OF CASES

CASE 1—V. G., a Negress aged 29, was admitted to the Harlem Hospital in December 1935, complaining of pain in the right groin, which had been present for two months. She had noticed a swelling in the area of the right femoral

⁹ Hartmann, H. *Rectites stenosantes*, in *Chirurgie du rectum*, Paris, Masson & Cie, 1931, pp. 166-239.

canal two weeks prior to admission. Physical examination showed her to be well developed and well nourished. The abdomen on palpation disclosed a mass in the right lower quadrant and tenderness over McBurney's point. Another mass, about the size of a walnut, was present in the area of the femoral canal, just below Poupart's ligament. It was fluctuant and freely movable. Bimanual examination revealed a mass which was thought to be a fibromyoma of the uterus, and the uterus was retroverted and in descensus. The pulse rate and the temperature were normal. The blood pressure was 134 systolic and 90 diastolic. The urine was normal. The white cell count of the blood was 11,400 per cubic millimeter, with 69 per cent polymorphonuclear leukocytes; the red cell count was 5,800,000 per cubic millimeter, with hemoglobin 80 per cent.

A roentgenogram of the chest was normal and the Kahn test of the blood gave a negative result. At operation the findings were a cyst of the right ovary, a retroverted uterus in descensus and a subacutely inflamed appendix with numerous adhesions. The ovarian cyst and the appendix were removed, and the uterus was suspended by the anterior suspension method of Coffey. An incision was then made over the femoral mass, which proved to be a well encapsulated abscess over Scarpa's triangle. It contained about 1 ounce (30 cc) of thick, yellow odorless pus. A small piece of the abscess wall was removed for study, and the cavity was packed with iodoform gauze. The pathologist reported that the tissue showed giant cells, with areas of necrosis, surrounded by epithelial cells in palisade arrangement. He made a diagnosis of lymphogranuloma.

The postoperative course was quiet. The midline incision (used for the intra-abdominal work) healed throughout its upper portion by primary intention. By the fourteenth day, a globular fluctuant mass the size of an orange had developed at the lower angle of the wound. This was incised and 2 ounces (60 cc) of odorless, watery pus was obtained. The patient was later discharged, with two draining sinuses—the unhealed abscess and the incised mass at the lower angle of the wound. Her general condition was good.

She was closely watched until November 1937. In spite of the negative Kahn reaction she was given antisyphilitic treatments. No improvement was seen. During this time walking became more painful, and the sinuses did not heal. She was then readmitted to the hospital. Except for the sinuses physical examination gave negative results. The temperature and the pulse rate were normal. The blood pressure was 120 systolic and 80 diastolic.

The blood count showed 7,200 white blood cells per cubic millimeter, with 70 per cent polymorphonuclears. There were 4,700,000 red blood cells per cubic millimeter, with a hemoglobin content of 70 per cent. The Frei test with human bubo antigen gave a positive result. Roentgenograms of the pelvis showed destruction of the intercartilaginous lamina and the pubic bone (fig 14). At operation each of the sinus tracts was probed and a free piece of cancellous bone was removed. The tract was completely excised with a Bovie knife. The free wound was closed without drainage. The excised tracts granulated to some extent, but there was no primary union. The patient was discharged on the sixteenth postoperative day, with some drainage from both tracts still present.

The pathologist reported that the specimen from one of the tracts showed only dead cancellous bone.

The patient's subsequent course has been observed. At the time of writing she is still having drainage from the sinuses. A roentgenogram taken in December

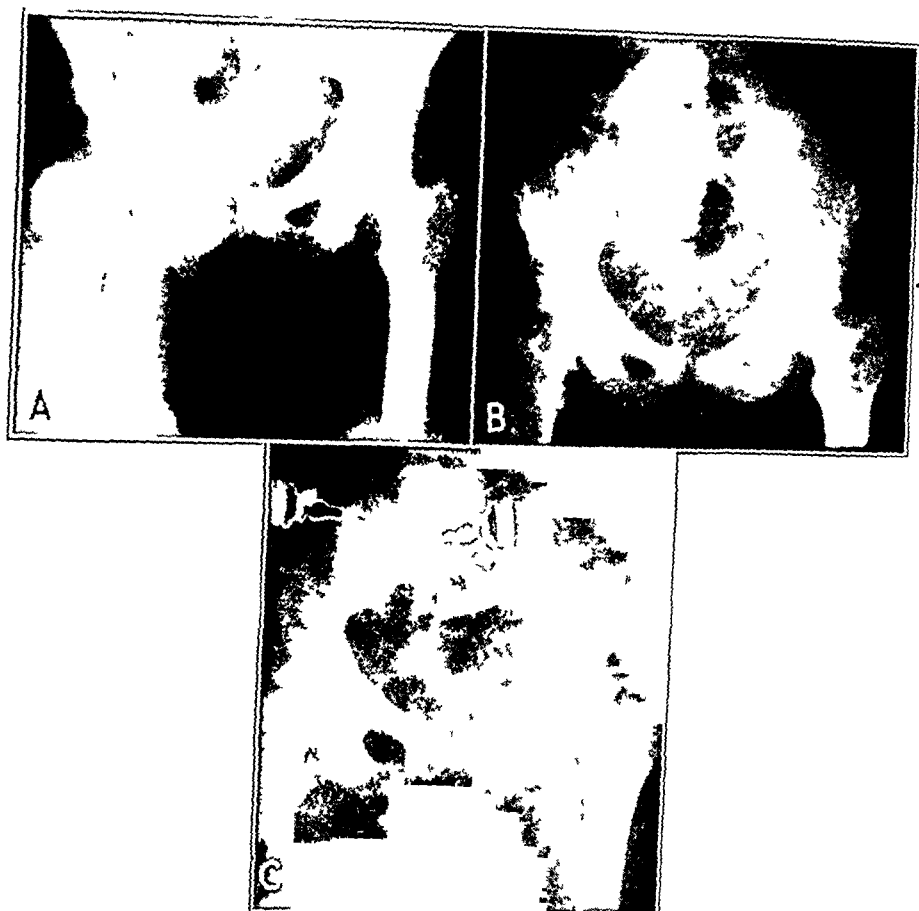


Fig 1 (case 1) —*A*, roentgenogram taken Nov 28, 1937, showing necrosis of bone at the symphysis pubis *B*, roentgenogram taken June 20, 1938. The process shows progressive destruction of the pubic bones *C*, injection of the abdominal sinus with iodized poppyseed oil

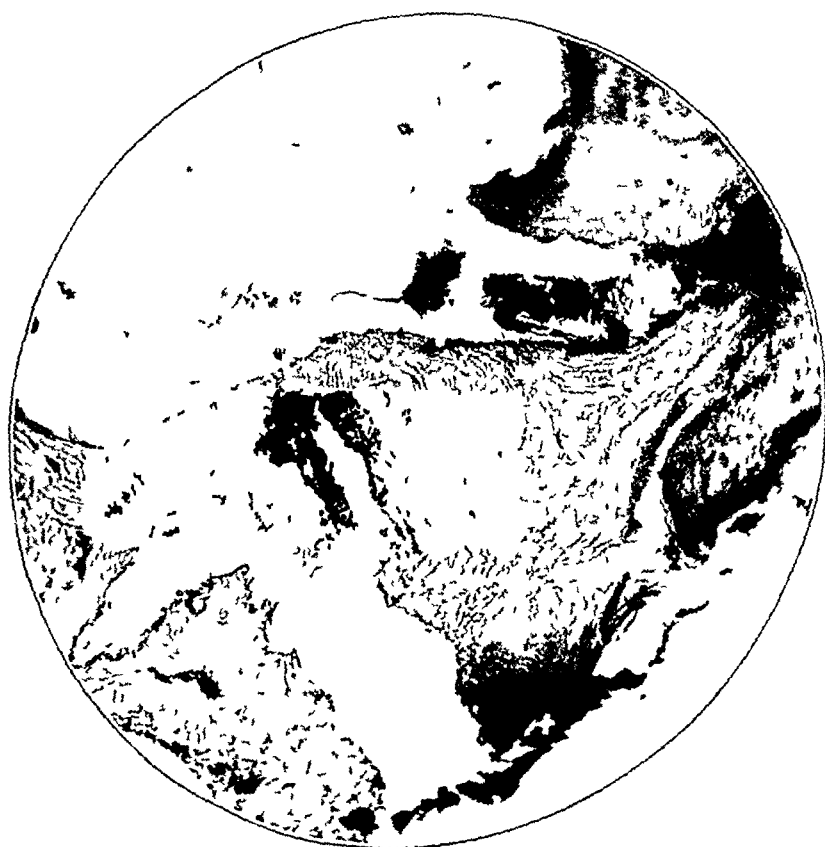


Fig 2 (case 1) —Photomicrograph of bone removed from the interior. Several pieces have been spontaneously extruded

1937 showed increase in the destructive process in the pubis. In February the process had spread more on the right side. Comparison of plates taken in June 1938 (fig 1B) and those taken in December 1937 shows the rapid progress of the destructive process. The Frei test was repeated in July 1938, with a markedly positive result. A roentgenogram taken on Sept 22, 1938 showed marked sclerosis in the region of both sacroiliac articulations. This was more marked on the left. There was no gross change in the process at the symphysis. A photograph taken on November 1 shows the appearance of the sinuses (fig 3).

Injection of iodized poppy seed oil into the orifice of the sinus of the abdominal wall showed the oil to escape from the inguinal sinus indicating a free communication between the two sinuses and the pubic area (fig 1C).

CASE 2—I G, a 39 year old housewife was admitted to the Harlem Hospital on June 28, 1938. Her complaints were difficulty in walking and weakness of the right leg. Pain had been present in the right hip joint and in the lower

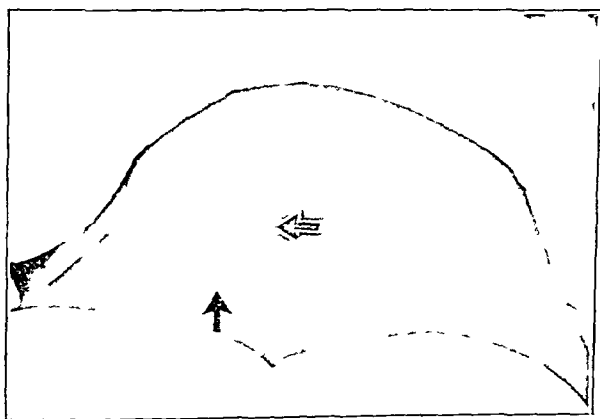


Fig 3 (case 1)—Position of the sinuses as they appeared on Nov 1, 1938

part of the back for three months prior to admission. This pain had been constant but had not prevented walking.

Her history included four previous admissions to the hospital. She dated her complaints from a hemorrhoidectomy done in 1926. After this operation she had sometimes been incontinent and had sometimes had pain on defecation. In 1930 she had had her only pregnancy which terminated in a spontaneous abortion at three months. Thick, odorous discharges from the rectum and vagina appeared in 1932. In January 1935 because of these discharges she was first admitted to the hospital.

Physical examination showed the patient to be poorly nourished. A rectal stricture which admitted only one finger was the only pathologic physical finding. The Kahn reaction of the blood was negative. The hemoglobin content was 70 per cent, and there were 4,000,000 red blood cells per cubic millimeter. The blood pressure was 98 systolic and 74 diastolic. The blood chemistry was within normal limits. A roentgenogram of the chest was normal. A colostomy was done, the proximal end of the sigmoid being used. An operative note stated that the area of rectal induration was thought to extend 7.5 cm above the pelvic diaphragm.

The patient's convalescence was uneventful, and she was discharged on February 18. Rectal resection was done on October 23, and at the same time a new anus was constructed. The pathologist reported that the rectal tissue showed "acute and chronic inflammation." The patient was again discharged. In September 1936, the colostomy opening was closed, with no subsequent morbidity. An incisional hernia developed and was repaired in December.

Physical examination in June 1937 showed the patient to be moderately well nourished. She was continent, and the stools were of normal size. A draining sinus was present on the mesial aspect of the left buttock. Physical examination disclosed no other abnormal signs. A Frei test with human antigen gave a markedly positive reaction. The Kahn reaction of the blood was negative and urinalysis showed no abnormalities. Roentgen examination showed destruction of the medial portions of the pubic ramus (fig 4).



Fig 4 (case 2) —Destruction of the medial portions of the pubic ramus. This lesion seemed to heal spontaneously.

Comment on Cases 1 and 2—These 2 cases fulfil the necessary requirements for a diagnosis of osseous changes due to lymphogranuloma venereum. The title of this paper was chosen because we have no desire to assert positively that the virus of lymphogranuloma venereum is the etiologic agent in the bone disease. On the other hand, the evidence for this relation seems to us to be strong. Tedder¹⁰ showed that when the involved lymph glands are surgically removed, there is an enormous amount of periglandular exudate. In case 1 biopsy disclosed the classic picture of the disease. The material was removed from the depth of the sinus, immediately adjacent to the necrotic bone. The fact that

¹⁰ Tedder, J. W. New Orleans M & S J 90 13 1937

osteomyelitis may be caused by infection of the adjacent soft tissue is not new. On the other hand the infection may have been borne directly into the bone by the lymphatics. The occurrence of pubic necrosis in both cases may easily be explained on the basis of the lymphatic distribution. Nesselrod's¹¹ recent study showed that 'in the female the lymphatic drainage from the external genitalia is inguinal, as in the male, but the drainage from the vagina and from the cervix is pelvic.' It is generally agreed that in 90 per cent of cases of lymphogranuloma venereum in females the original infection is cervical or occurs in the posterior portion of the vagina and rectal stricture results, the lymphatic drainage being posteriorly. The patient in case 1, we think, had the initial lesion on the clitoris or the external part of the vulva (upper margin of the labia). A massive infection spreading both anteriorly and posteriorly must be postulated for the second case, in which there were a rectal stricture and a pubic lesion. Martin¹² stated that in his experience 90 per cent of females are afflicted with rectal stricture while only 10 per cent have involvement of the genitalia and the inguinal glands. For males these figures may be reversed but in either sex both may exist simultaneously. This is true in our experience. We have gone to great pains to eliminate other possible etiologic factors, and it is our belief that these 2 cases represent definite bone changes due to lymphogranuloma.

CASE 3.—W. W., a 53 year old Negro, was admitted to the Harlem Hospital on July 8, 1938, complaining of pain in the lumbar portion of the spine and in both hip joints, which had been present for one year. For six months prior to admission it had been more severe; it was worse on motion in dry weather and during the day. It was relieved by salicylates. She had been taking codeine in doses of unknown size for relief of the pain. There had been nodules on the inner aspect of the right thigh and just below the jaw. These had disappeared before admission. Her past history showed that at the age of 23 the cervical lymph nodes on the left were removed because of chronic enlargement. In 1923 a colostomy was done in the New York Hospital because of rectal stricture. Antisyphilitic treatments were begun at that time. In May of that year a retrovaginal fistula developed, which was excised at the same institution. The rectal stricture was then dilated. In the three subsequent years three abscesses developed around the colostomy opening, these were opened. In 1930 the patient again entered the New York Hospital, where a cecostomy was done. Between 1921 and 1929 antisyphilitic treatment was given at intervals. In 1932 a discharging sinus developed over the sternum and one over the tenth dorsal vertebra in addition to generalized adenopathy. In spite of the now negative Wassermann and Kahn reactions a diagnosis of tertiary syphilis was made because of the sinuses. She was treated with a bismuth compound and sodium thiosulfate. The patient was admitted to the Harlem Hospital in 1936 for the first time (fig. 5). There was an ulcer

11 Nesselrod, J. P. Demonstration of Genito-Ano-Rectal Lymphatics. *Tr. Am. Proct. Soc.* **36**: 85, 1935.

12 Martin, C. The Variety and Distribution of Groin Lesions in Lymphogranuloma Venereum. *Tr. Am. Proct. Soc.* **37**: 72, 1936.

of the soft tissues over the sternum and necrosis of the bone under it. There was an area of erythema around the ulcer, which varied from 3 to 5 cm in depth. The colostomy opening, which evidently had been made in the transverse colon, had contracted to the size of a lead pencil. The liver and spleen were palpable. A roentgenogram of the sternum showed destruction above the junction of the



Fig 5 (case 3) —Lesion over the sternum as it appeared June 10, 1936. Note the operative scars and the hernia, indicative of multiple colostomies for a rectal stricture.



Fig 6 (case 3) —Photograph taken on July 12, 1938. The sternal lesion is still present.

manubrium and the body of the sternum. The Kahn test of the blood gave a negative result.

Bacteriologic examination of the fluid from the sinuses over the sternum and those of the back did not reveal tubercle bacilli or actinomycetes. The blood pressure was 116 systolic and 78 diastolic. The blood count showed 7,500 white

cells per cubic millimeter, with 67 per cent polymorphonuclears and 33 per cent lymphocytes. There were 4,010,000 red blood cells per cubic millimeter and a hemoglobin content of 60 per cent. Urinalysis showed a specific gravity of 1.012, a 2 plus reaction for albumin, granular and hyaline casts, white blood cells and urates. The temperature on admission was 98.2 F, and the pulse rate was 84. The temperature rose at intervals during the patient's stay in the hospital to 100.8 F. Specimens of the soft tissue and of the bone from the ulcer showed, on pathologic examination, a chronic inflammatory process.

Physical examination in 1938 showed the patient to be poorly nourished. The mucous membranes were pale. The abdomen showed cecostomy and colostomy scars and two draining sinuses. The sternal sinus was still present (figs 5 and 6). There were marked kyphosis and moderate scoliosis. A roentgenogram of the pelvis was normal. The dorsal portion of the spine showed fusion of the fourth and fifth and of the tenth and eleventh thoracic vertebrae, with destruction of the intervertebral disks and compression of the tenth and eleventh vertebral bodies. Examination of the chest gave negative results but the spinal lesion seemed to be tuberculous.

Comment on Case 3—The patient had lymphogranuloma venereum, tuberculosis and syphilis. She showed no improvement after protracted antisyphilitic therapy. The tissue removed from the ulcer did not show tuberculosis or syphilis. For these reasons we believe that the inflammatory process as studied clinically and pathologically was caused by lymphogranuloma venereum. This case does not meet the diagnostic requirements that were laid down as prerequisites for a diagnosis of osseous disease due to lymphogranuloma venereum. Because of the presence of tuberculosis and syphilis, one cannot say with certainty that the lesion of the sternum was due to lymphogranuloma, but it is highly probable that it was.

SUMMARY

There is much evidence of the constitutional nature of infection with lymphogranuloma venereum and for this reason it is not surprising that late involvement of the osseous system can occur. Systemic reactions occurring early in the disease, such as anorexia, nausea, vomiting, chills and fever are mentioned by most authors. Injections of the virus into laboratory animals cause lesions of different systems depending on the method of inoculation. For example intraperitoneal injection causes exudative peritonitis; intracerebral injection has produced meningoencephalitis; subcutaneous preputial injection of the virus is followed by involvement of the regional lymph nodes. The virus has been isolated from the mesenteric glands, spleens, livers and lungs of infected animals. It has rarely been demonstrated in the blood. In human beings extragenital lesions have been reported as occurring on the tongue. Splenic enlargement has been noted. David and Loring¹³

¹³ David V. C. and Loring M. Extragenital Lesion of Lymphogranuloma Venereum. *Inguinale*, J. A. M. A. 106:1875 (May 30) 1936.

reported a case of lymphogranuloma venereum causing ulcers in the mouth and colon. They stated the opinion that lymphogranuloma venereum should be considered a possible etiologic factor, as in all cases of meningoencephalitis of obscure origin. Von Haam and D'Aunoy¹⁴ successfully isolated the virus from the spinal fluid in cases of lymphogranuloma venereum. They quote Smood¹⁵ and his associates as follows: "In some cases infection with the virus of lymphogranuloma inguinale simulated rheumatic fever, with the pain and inflammatory reactions occurring in large and small joints."

In regard to the mechanism of virus action, Rivers¹⁶ stated

If the action of the viruses is not extremely rapid or explosive and if the susceptible cells are capable of multiplication, the primary effect of the active agents is stimulation, leading to cellular hyperplasia. Following the hyperplasia there is usually destruction or necrosis of the cells, which, in turn is attended or followed by a secondary inflammation representing the reaction of the neighboring tissues and the host. The balance between the stimulative and destructive tendencies of the viruses determines whether hyperplasia or necrosis is the predominant part of the pathologic picture. If the action of the viruses is explosive or rapid, as, for instance in Yellow fever and Rift Valley fever, or if the susceptible cells are incapable of division and multiplication, as is the case with nerve cells, then the primary pathologic changes are necrobiosis and lysis of cells.

Lymphatic involvement with perilymphatic reaction is a possible explanation of the destructive lesions of the pubes in cases 1 and 2. The close proximity of the inguinal glands, with their massive infection to the pubes, suggests the possibility that the infection spread by direct extension.

If one considers that most lesions of lymphogranuloma are genital in origin, some adequate explanation must be found for the infection of joints as anatomically distant as the wrist and knees. The mechanism of this spread has not been demonstrated so far.

Our cases have been like the others reported in that there has been no uniformity in the period elapsing between the initial infection and the occurrence of lesions in the bones. Coutts and Banderas Bianchi¹⁷ mentioned the occurrence of arthritis during the second week of the disease. In Reichle and Connor's case the articular symptoms occurred only four months after the onset of the infection. Frauchiger considered that chronic arthritis was present in the cases that he reported. In all of our cases the condition was definitely chronic.

14 von Haam, E, and D'Aunoy, R. Is Lymphogranuloma Inguinale a Systemic Disease? *Am J Trop Med* **16** 527, 1936

15 Smood, cited by von Haam and D'Aunoy¹⁴

16 Rivers, T. M. Pathologic and Immunologic Problems in the Virus Field. *Am J M Sc* **190** 435, 1935

17 Coutts, W. E., and Banderas Bianchi, T. Lymphogranulomatosis Venerea and Its Clinical Syndromes, *Urol & Cutan Rev* **38** 263, 1934

The literature reporting osseous and articular lesions associated with lymphogranuloma venereum has been critically examined. In the early phases of the disease arthritic and polyarthritic manifestations may occur, although they are not especially common. Chronic arthritis may occur late in the disease. Except for cases of arthritis, hydrarthrosis and pyoarthrosis, no instances of actual destruction of bone was found. We report 2 apparently proved cases of bone necrosis associated with lymphogranuloma venereum and a third case, in which such an association is highly probable. Comments have been made on the theoretic considerations of bone lesions in this disease. Minimum diagnostic criteria have been presented, which it is hoped will aid further study of the problem of osseous changes associated with lymphogranuloma.

CONCLUSION

Osseous changes in lymphogranuloma venereum are rare, may occur late in the disease and are probably caused by the specific infection. Joints and flat bones are most frequently involved.

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FRONTAL PUNCTURE FOR VENTRICULOGRAPHY

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We are well aware that some neurosurgeons occasionally perform ventriculographic examination through frontal burr holes,¹ however, the numerous advantages of the method have not been sufficiently stressed and it does not at present enjoy the widespread use it deserves. For this reason the following note is submitted.

Since ventriculography was first described² the method of choice for ventricular puncture in most clinics has been to make a parieto-occipital opening in the skull³ and to insert the brain cannula into the ventricular system either in the posterior horn or at the junction of the posterior horn with the body. Difficulties met with in this procedure may be enumerated as follows:

1 The posterior horn in normal persons varies considerably in size. In some cases it may even be absent. Numerous cannula punctures may be necessary before the ventricle is reached.

2 The cannula may enter the glomus of the choroid plexus and produce a hemorrhage into this structure. This produces a misleading or confusing intraventricular filling defect.

3 All too frequently in the interchange of gas for fluid poor filling of the third ventricle results, and the aqueduct and fourth ventricle are not visualized. This is due to the fact that the cannula is in a lateral ventricle at the level of or above the foramen of Monro, and the fluid which is removed is only that from the ventricle tapped plus that from the portion of the opposite ventricle anterior to and above the foramen of Monro (fig 1 A).

4 The need for bilateral ventricular puncture is frequent.

1 Dandy, W E. Cerebral Pneumography, in Lewis, D. Practice of Surgery, Hagerstown, Md, W F Prior Company, Inc, 1936, vol 12, chap 1, p 89.

2 Dandy, W E. Ventriculography Following the Injection of Air Into the Cerebral Ventricles, *Ann Surg* 68 5, 1918.

3 Horrax, G, in Nelson Loose-Leaf Living Surgery. New York: Thomas Nelson & Sons, 1937, vol 11, p 416N. Deery, E M. A Method of Ventriculography, *Bull Neurol Inst New York* 1 193, 1931.

5 The cannula tract is close to the visual pathways, and blindness⁴ (usually temporary) following posterior ventricular puncture is not unknown

6 In hospitals where ventriculographic examination is not a frequent procedure, adequate operating tables or chairs with proper head rests are not always available

Frontal ventricular puncture is performed as follows

The entire head is shaved and prepared. With the patient in the prone position with the head extended, a 3 cm incision is made just within the hair line above the forehead (10 cm above the supraorbital ridge) and 2 cm lateral and parallel to the midline. The skin and subcutaneous tissues are retracted with a mastoid retractor, which also controls the bleeding. A burr hole or trephine opening is made in the bone. The outer layer of the dura is incised with a sharp-pointed

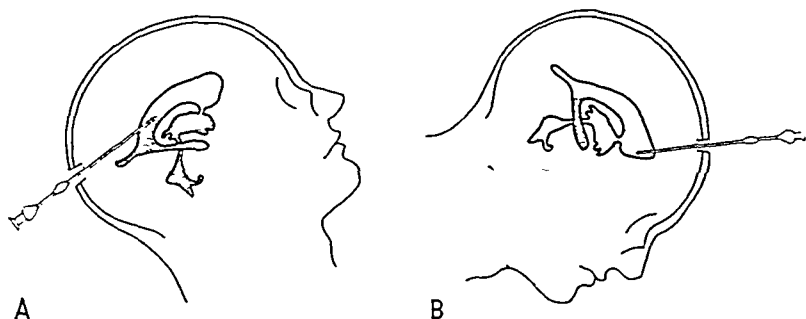


Fig 1—*A* posterior ventricular puncture. The ventricle is tapped at the level of the foramen of Monro. *B* frontal ventricular puncture. The ventricle is tapped below the foramen of Monro.

scalpel, the edge being grasped and retracted with mosquito forceps. This permits the opening of the inner layer of the dura with greater safety and prevents injury to the underlying cortex. The dura is then opened widely. A small nick is made with the scalpel through the leptomeninges and the pia in the center of a gyrus. The brain cannula is then inserted perpendicular to the surface of the skull and slightly mesially. The lateral ventricle is entered at the junction of the anterior horn with the body. By this method as compared with the posterior approach the ventricle is entered with remarkable ease. It is only on rare occasions that more than one needle puncture is necessary. The needle is below the foramen of Monro (fig 1 *B*) and consequently in this procedure most of the fluid of the entire ventricular system

⁴ Masson C B. Disturbances in Vision and in Visual Fields After Ventriculography. *Bull Neurol Inst New York* 3:100, 1933.

(including the third ventricle, the aqueduct and the fourth ventricle) can be replaced through this single burr hole

The advantages of this method of frontal ventricular puncture are the following

1 There is little variation in the anatomy of the ventricular system at the point where the cannula enters it, in contradistinction to the great variation found in the size of the posterior horns. More than one cannula puncture is rarely necessary

2 The choroid plexus is avoided

3 Much better visualization of the entire ventricular system is afforded



Fig 2—Patient in position for frontal ventricular puncture. The cerebellar head rest is in the reverse position

4 The need for bilateral ventricular puncture is lessened

5 There is less chance of injuring important cerebral structures

6 When the patient is in the prone position the intraventricular pressure is higher than when he is in the semirecumbent or sitting position, thus more complete drainage of the ventricular system is obtained

7 No special operating tables, chairs or head rests are necessary. If a cerebellar head rest is available it is best to reverse it and extend the patient's head (fig 2). We have frequently used an ordinary operating table, the patient's head being extended by means of a sand bag or a hard pillow placed beneath the chin.

DRAINAGE OF THE COMMON BILE DUCT WITH RESULTANT EXTRARENAL AZOTEMIA

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AND

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This paper is presented to describe a comparatively rare complication following drainage of the common bile duct. On reviewing the literature we found few data on the actual amount of biliary drainage to be expected from a T tube after exploration of the duct. In our experience the average figures for an adult are 300 to 500 cc per day with a maximum of 1,500 cc in an isolated instance. Other investigators have placed a high point at 25 to 30 cc per kilogram of body weight per day, which for an average person weighing 75 Kg would amount to 2,250 cc daily. Walters and his associates¹ in their paper on cholorrhagia following prolonged obstruction reported an output of 2,050 cc in a single day in 1 patient. In the case here presented there was much more abundant drainage, starting at 1,800 cc on the first postoperative day.

REPORT OF A CASE

E K, a 57 year old white man, was admitted to the State of Wisconsin General Hospital on Jan 27, 1938. The chief complaint was pain in the stomach. After a fall on Sept 11 1937 he had acute paroxysmal abdominal pain, a temperature of 105 F and jaundice. After a week he was discharged from his local hospital a blind, fat-free diet being prescribed. At this time the jaundice was clearing. Similar attacks followed with increasing frequency until late in December, when jaundice appeared and persisted. Administration of morphine was necessary for relief of pain in all episodes. Fever was present on each occasion. The color of the stools definitely changed as the jaundice increased or regressed.

The history by systems revealed no pertinent symptoms except a loss of 50 pounds (22.5 Kg) in the preceding four months. The family history and the social history were essentially noncontributory.

Physical examination showed moderate icterus of the skin and sclera and evidences of recent scratching. The chest was barrel shaped and hypereminent with bilateral basal rales posteriorly. The heart tones were distant and the heart was slightly enlarged to the left with a soft systolic murmur at the apex which was transmitted to the axilla. The blood pressure was 120 systolic and 82

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1 Walters, W., Greene, C. and Friedrich, C. Complications Following Relief of Biliary Obstruction. *Ann. Surg.* 91 (8): 93 (Nov) 1930.

diastolic Abdominal examination revealed the liver 4 cm below the right costal margin, with a questionable mass in the area of the gallbladder Murphy's sign was present The reflexes were intact Rectal examination showed prostatic hypertrophy, grade 3

Laboratory Findings—The urine was essentially normal except for the presence of bile The value for hemoglobin was 13 Gm per hundred cubic centimeters The red blood cell count was 4,410,000 The white blood cell count was 9,950, with 87 per cent neutrophils, which showed evidences of toxic degeneration The icteric index was 45 The sugar content of the blood was 93 mg and the non-

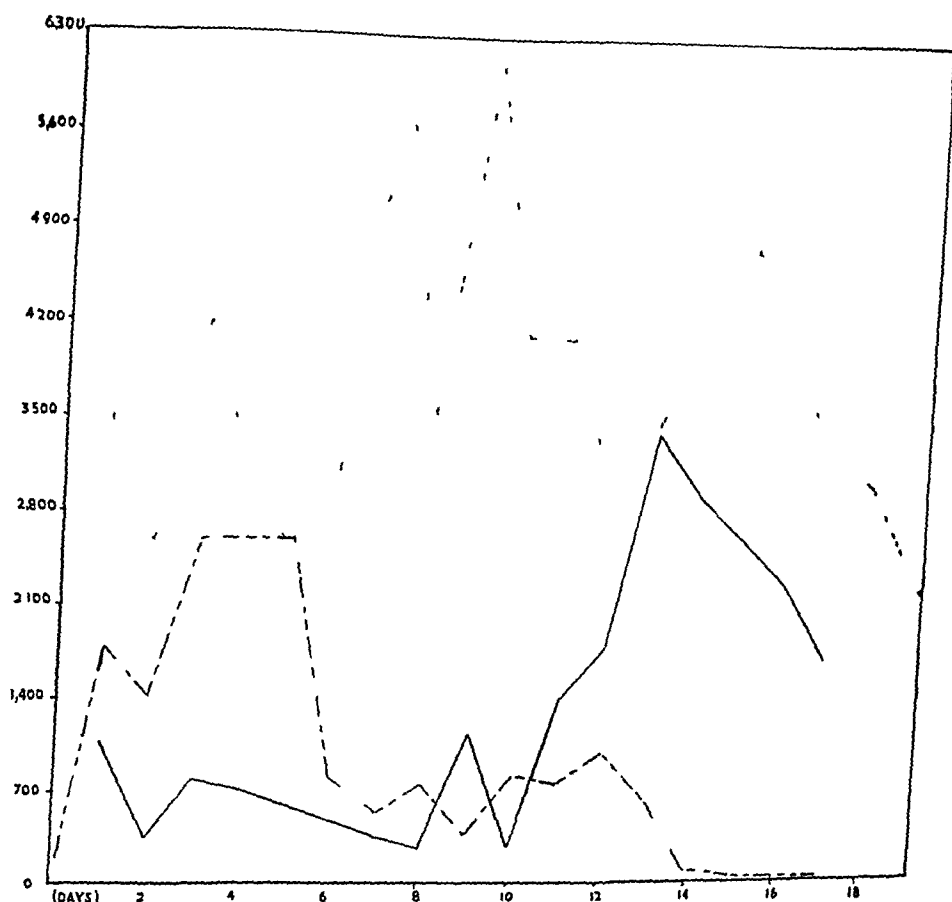


Chart 1—Graphic representation of output of bile (line composed of one long and two short dashes alternately), intake of fluid (evenly broken line) and output of urine (solid line)

protein nitrogen content 33 mg per hundred cubic centimeters The Wassermann reaction of the blood was negative The value for serum protein was 6 Gm (albumin 39 and globulin 21 Gm) The albumin-globulin ratio was 19 The sedimentation rate was 27 mm in sixty minutes

Röntgen Studies—A flat roentgenogram of the abdomen showed no radiopaque bodies The gastrointestinal series showed an old ulcer in the pyloric canal

The impression was of obstruction of the common duct due to stone It is agreed that exploration after surgical preparation was indicated By February 4 the icteric index was 25, the stools contained bile and the sedimentation rate was 23 mm in one hour On February 10 the abdomen was explored by open method

(K E L), with the following findings and operative procedure "There were many adhesions in the right upper quadrant of the abdomen, and the pylorus and duodenum were freed with some difficulty from the mass around the gallbladder. The latter was finally freed and the gallbladder and cystic duct were found to contain stones. Stones were also palpable in the common duct. The gallbladder was removed retrograde and severed at the junction of the ampulla and the cystic duct. Through this opening five small stones and one large stone were removed. Probes could then be easily passed up into the right and left hepatic ducts and down into the duodenum, and the system was flushed with physiologic solution of sodium chloride. After this a T tube was sutured in place in the common duct and a cigaret drain was placed in the gallbladder bed. The wound was closed in layers in the usual manner."

Postoperatively the patient's course seemed satisfactory except that as early as the first day after the operation it was noted that unusually large amounts of bile

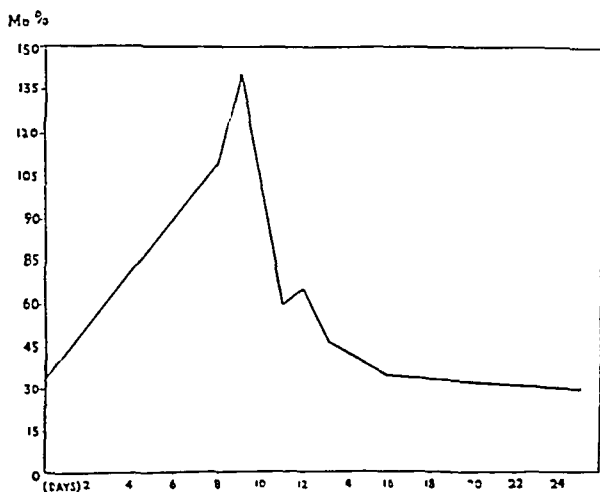


Chart 2—Nonprotein nitrogen

were draining through the tube in the common duct. An attempt was made to control this by means of gradual decompression as suggested by Raydin and Frazier.² This was done by raising the level of the drainage bottle to the height of the patient's bed thus preventing a siphon-like action. In spite of this procedure drainage of bile amounting to from 1800 to 2600 cc per day began almost immediately (chart 1). This contrasted markedly with the 300 to 500 cc observed in most cases but in view of the patient's apparent well being we were not unduly alarmed. Liquids were being taken by mouth but greater amounts of fluid were being lost by biliary drainage. By the sixth day drowsiness, anorexia and fear of impending death ensued and the patient began to vomit. The carbon dioxide-combining power determined the following day was 26.8 volume per cent (charts 2 and 3).

² Raydin I S and Frazier W D. Advantages of Gradual Decompression Following Complete Common Duct Obstruction. *Surg Gynec & Obst*, **65**: 1115 (July) 1937.

The nonprotein nitrogen content had risen to 109 mg per hundred cubic centimeters, with a creatinine content of 27 mg per hundred cubic centimeters. Therefore the fluid intake was raised to 5,960 cc, given by the oral and parenteral routes, including 160 cc of a solution of sodium lactate. To complicate the picture further, Wangensteen's negative gastric suction had to be started the next day to control the vomiting. The alkali reserve on the eighth day rose to 39.5 volumes per cent. With the decrease of the alkali reserve it will be further noted that the output of bile decreased to 400 to 800 cc between the sixth and the ninth day postoperatively. Despite a high fluid intake the patient excreted little urine on the seventh and eighth days, so that dehydration apparently complicated the acidosis.

The chloride content of the blood was not determined until the eighth day after operation and at that time it was 403 mg per hundred cubic centimeters. It will be seen (charts 1 and 2) that the nonprotein nitrogen content and the carbon dioxide-combining power rapidly returned to normal as the output of bile continued

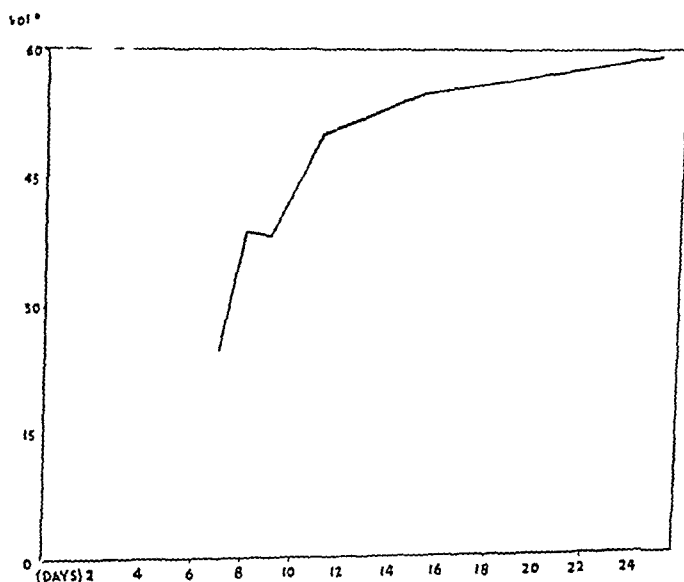


Chart 3—Carbon dioxide-combining power

to decrease and the output of urine increased, and the patient returned to a position of positive fluid balance.

COMMENT

It has long been contended that the syndrome of *cachexia cholepriva* is dependent, at least in part, on the acidosis caused by the loss of sodium salts of the bile acids in the presence of complete biliary fistulas. Okada,³ McMaster and his associates,⁴ Neilson and Meyer⁵ and finally Drury

3 Okada, S. On the Secretion of Bile, *J. Physiol.* **49** 456-482 (Aug.) 1915

4 McMaster, P. D., Broun, G. O., and Rous, P. Studies on Total Bile, on the Bile Changes Caused by a Pressure Obstacle to Secretion, *J. Exper. Med.* **37** 685-698 (May) 1923

5 Neilson, N. M., and Meyer, K. F. Reaction and Physiology of the Hepatic Duct and Cystic Bile of Various Laboratory Animals *J. Infect. Dis.* **28** 510-541 (May-June) 1921

and his associates⁶ with studies on the p_H of bile emphasized the fact that it is a well buffered solution and that considerable amounts of acid are necessary to change its reaction. In this connection Wangenstein showed a patient with total biliary obstruction who was losing only 0.4 Gm of sodium chloride daily in the bile.

The conclusive experiments of Bissell, Andrews and Brunswick⁷ showed that the carbon dioxide-combining power in cases of complete biliary fistula does not change at least experimentally. Eight dogs with an average carbon dioxide-combining power of 39.5 volumes per cent and an average value for blood chlorides of 290 mg per hundred cubic centimeters were used, and a cholecystnephrostomy was done or a permanent biliary fistula produced. After this the animals were studied for periods ranging from twelve to eighty days. The symptoms of acholic cachexia were typical, but the carbon dioxide-combining power averaged 39.5 volumes per cent and the chlorides 293 mg per hundred cubic centimeters. On the subject of acid-base equilibrium they said in conclusion:

It seems justified therefore, to assume that if the typical picture of cachexia cholipriva may be produced without changes in the acid-base equilibrium this factor is not fundamental and that when reported by others it must be assigned to some intercurrent or indirect cause and must not be considered a fundamental etiologic factor. While acidosis, as reported by many, may be a frequent accompaniment of acholic cachexia and may explain some of its manifestations, it seems wisest to attribute it to infection of the fistulous tract rather than to loss of bile.

Latteri⁸ has also reported changes in the carbon dioxide-combining power after experimental studies on the biliary tracts of dogs. This work shows definite decrease in the carbon dioxide-combining power following complete occlusion of the common bile duct. It is not, however, applicable to studies on animals or on subjects with biliary fistulas.

In our case the picture was typical of acidosis, sometimes referred to as extrarenal azotemia, and this was substantiated by a low carbon dioxide-combining power of 26.8 volumes per cent. However, the factor of infection with positive cultures of *Bacillus coli* and unidentified streptococci from the bile on the eighth day, must be taken into account.

An attempt to explain the entire picture of acid-base disturbance necessitates the consideration of several factors. As early as the fifth

6 Drury, D., Rous, P. and McMaster, P. D. Observation on Some Causes of Gall Stone Formation. *J. Exper. Med.* **39**: 403-423 (March) 1924.

7 Bissell, A. D. and Andrews, E. Acholic Cachexia. Experimental Studies. *Arch. Surg.* **32**: 624-668 (April) 1930. Andrews, E. and Bissell, A. D. Acholic Cachexia. Acid-Base Equilibrium. *Proc. Soc. Exper. Biol. & Med.* **31**: 548-550 (Feb.) 1934. Brunswick, A., Bissell, A. D. and Andrews, E. Acholic Cachexia. Pathological Changes. *ibid.* **32**: 41-42 (Oct.) 1934.

8 Latteri, S. La riserva alcalina nelle stenosi ed occlusioni sperimentali delcoledoco. *Ann. ital. di chir.* **10**: 60-83 (Feb. 1-) 1931.

postoperative day there was a sense of malaise, and the next day there were frank mental lethargy and drowsiness. The total output of bile during the first six days was 12,800 cc. Urinary excretion steadily decreased to a low point of 310 cc, suggesting approaching anuria. We believe that usually with an alkali deficit the kidneys respond with a greatly accelerated elimination of water and acid and the formation of large amounts of ammonia. In this manner a large amount of the water of the body is excreted. We feel that diuresis and dehydration are part of the phenomena consistently accompanying acidosis in the absence of renal disease. It is true that in this case in contrast to diuresis there was a reduction of the urinary output, but this can be accounted for by the excessive amount of fluid lost through biliary drainage and vomiting.

Peters and Van Slyke⁹ disagreed with the statement in Marriott's monograph on anhydremia, that acidosis is one of the phenomena of dehydration. It was difficult for them to see how dehydration can in itself cause an alkali deficit unless the anuria interferes with the renal excretion of ammonia and acid. "In this case one might expect an acidosis similar in nature to that of nephritis. Whether such retention follows dehydration appears not to have been determined."

The negative fluid balance, which was present for several days, amounted at times to 300 to 400 cc. This complication was suggested by Snell and Rowntree, who said that secretion of bile is independent of conditions of fluid intake and electrolyte balance. McMaster, Brown and Rous⁴ have shown that after relief of obstruction the output of bile is copious until the elimination of retained biliary constituents has been completed. The bile in this period is much more dilute than normal, but, by the increase in volume, output of bile pigment is elevated during the period of cholelithiasis.

SUMMARY

In our opinion this case emphasizes three facts

- 1 The elimination of large amounts of bile through a fistula, at least in the presence of infection, may cause acidosis
- 2 Copious drainage of bile may follow drainage of the common duct for obstruction in spite of biliary decompression
- 3 Accurate records of total fluid intake and output must be kept in order to eliminate the danger of a negative fluid balance as a factor in the production of acidosis

⁹ Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry*. Baltimore, Williams & Wilkins Company, 1931, vol. 1.

FATE OF BURIED SKIN GRAFTS IN MAN

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NEWARK, N. J.

Present opinion hypothesizes that epithelium-lined cysts often occur from portions of surface epithelium transplanted into the deeper tissues beneath the skin. This transplantation is believed to follow puncture wounds of the palm and fingers the point of an instrument or tool having carried a small piece of surface epithelium into the deeper tissues. It is assumed that the small piece of epithelium forms an epithelium-lined cyst which is stimulated to active growth by any form of irritating secondary trauma.

Many investigators have performed experiments on animals by burying strips of epidermis and full thickness skin. In these experiments cysts were observed originating from the epidermis and from the hair follicles. In man, so far as is known the investigation has been limited to the study of traumatic epithelial cysts presumed to result from injury or operative incision. My observations in microscopic examination of skin buried in human beings differ from the observations of investigators working with animals.

PREVIOUS EXPERIMENTAL WORK

Reverdin¹ expressed the belief that as a result of trauma bits of epidermis are torn off and deposited deep in the corium and that cysts develop from these implanted grafts.

Garre,² stated that implantation of epidermis alone produces a smooth-walled cyst, while in the cyst resulting from implantation of a whole thickness skin graft papillae are also present.

Kautmann³ produced a cyst beneath the skin of the cock's comb by making a deep oval incision through the skin and suturing the margins of the skin together over the oval section. The buried epidermis gradually took on a rounded form and invariably developed into a cyst. The

Presented before the Society of Plastic and Reconstructive Surgery at the New York Academy of Medicine March 24 1938

1 Reverdin J. L. Des kistes epidermiques des doigts. Rev. med. de la Suisse Rom. **7** 121 1887

2 Garre C. Ueber traumatische Epithelcysten der Finger. Beitr. z. klin. Chir. **11** 524 1894

3 Kautmann F. Ueber Enkystung von Epithel. Virchow's Arch. f. path. Anat. **97** 236 1884

origin of this cyst from the epidermis was evident, because the cock's comb contains no hair follicles or granular elements to provide another possible source

Schweninger,⁴ in a similar experiment on dogs, produced subcutaneous cysts by burying a piece of skin below the surface. Some of the cysts so produced contained hairs and sebaceous glands in their walls and fat, cholesterol and epidermal scales within their lumens.

Pels-Leusden⁵ suggested another possible origin for the epithelial cyst and supported it by experiments on the ears of rabbits. He made an incision through the skin, using a "sharp knife" to prevent the accidental implantation of epidermis during the operation. He then placed an absorbable magnesium disk deep within the corium. A cyst was produced about the foreign body, the lining membrane of which contained all the layers of normal epidermis. Pels-Leusden expressed the belief that such a cyst is formed by proliferation from the epithelium of glands that are unavoidably injured by the incision. He concluded that it is unlikely that in an ordinary injury the tough skin of the palm could be torn off and implanted.

Hesse,⁶ in a series of experiments, buried a magnesium disk, catgut and a blood clot beneath the skin and later examined histologic serial sections of the sites of implantation. He demonstrated that epithelization to produce a cyst may take place from the hair follicles and the glandular epithelium without any apparent burial of epidermis. He was unable to find papillae in the walls of any of the cysts produced, however, and he stated that for the development of papillae the implantation of whole thickness skin was necessary.

Davis and Traut⁷ produced epithelium-lined tubes and sacs in dogs by transplanting free grafts of whole thickness skin directly onto one of the abdominal muscles. In each animal the fascia was drawn over the graft and the graft was left in place from twenty to forty days. The animal was killed, and the buried skin with the adjacent structures was carefully removed and fixed in solution of formaldehyde. The authors noted the formation of an epithelium-lined tube or cyst resulting from a cylindric growth at the margins of the skin graft. They stated that when the experiments were carried beyond forty days maceration of the epithelial lining of the cavity of the cyst occurred.

4 Schweninger, E. Beitrag zur experimentellen Erzeugung von Hautgeschwulsten (Atheromen), *Charité-Ann* **11** 642, 1884.

5 Pels-Leusden, F. Ueber abnorme Epithelisierung und traumatische Epithelcysten, *Deutsche med. Wchnschr* **31** 1340, 1905.

6 Hesse, F. A. Die Entstehung der traumatischen Epithelcysten, *Beitr. z. klin. Chir* **80** 494, 1912.

7 Davis, J. S., and Traut, H. F. The Production of Epithelium Lined Tubes and Sacs, *J. A. M. A* **86** 339 (Jan. 30) 1926.

They assumed that this was due to pressure from the contents of the cyst. Histologic observations on the state of hair follicles and glandular elements in the dermis of the skin graft were not reported.

Zimches⁸ in a series of his own experiments and in experiments performed in association with Wassiljew, buried free strips of full thickness skin in the muscle of dogs. His conclusions, based on studies of implants buried for periods up to two years, were as follows:

1 The epidermis of the implanted skin curves in the shape of a horseshoe and on about the twenty-fifth day the ends of the horseshoe join forming a circle or closed cavity lined with epithelium.

2 The cavity of the cyst is partly filled by epithelial debris and broken-down hairs.

3 The cyst continues to grow because the lining epithelium constantly produces cornified epithelium, which is pushed into the lumen.

4 Small cysts may develop from the epithelium of hair follicles.

5 The tendency of surface epithelium when transplanted into other tissue to bend on itself and form a closed cavity represents a definite law and finds its explanation in the general law of epithelial growth.

6 Changing of one kind of epithelium into another or into malignant tissue was not observed.

7 The implanted section of skin heals in its new position and quickly joins the surrounding tissue by means of granulation tissue, which is later organized into connective tissue.

The occurrence of foreign body giant cells in the unlined wall of an epidermal cyst has been explained by Stewart.⁹ According to him, the contents of the cyst whether composed of hair, fat, cholesterol or epithelial debris have the irritant properties of a foreign body. In those parts of the cyst where the epithelial lining is lacking this irritation produces a type of granulation tissue rich in giant cells.

Wien and Caro¹⁰ stated that the traumatic epithelial cyst is believed to develop as a result of injury to the skin and occurs most frequently on exposed sites such as the palms and fingers. The probable origin of the cyst is from epidermis torn from the surface and carried into the corium. Such a cyst may also form about a foreign body implanted into

8 Zimches, J. L. Ueber das Schicksal des in die tieferen Gewebe frei transplantierten Deckepithels in Zusammenhang mit der Lehre von den Epithelcysten. Frankfurt Ztschr. f. Path. **42**: 203, 1931.

9 Stewart, M. I. On the Occurrence of Irritation Giant Cells in Dermoid and Epidermoid Cysts. J. Path. & Bact. **17**: 502, 1912.

10 Wien, M. S. and Caro, M. R. Traumatic Epithelial Cysts of the Skin. J. A. M. A. **102**: 107 (Jan. 20), 1934.

the dermis by proliferation of epithelium from the hair follicles or glandular elements of the skin

Imakita¹¹ transplanted particles of skin into the muscle tissue of guinea pigs and noted that hypertrophy and hyperplasia of epidermis and hair follicles were more marked in muscle tissue than in brain. As in his earlier experience with guinea pigs, almost all implants formed cysts at the end of two weeks, and even five months after implantation the epidermis was thicker than in the control section. In a subsequent article¹² the same author came to the same conclusions by counting the mitotic figures.

Okuma¹³ buried sections of skin the size of a rice grain in the subcutaneous fasciae of the backs of adult rabbits. The implanted particles of skin invariably caused the formation of a cystlike structure after a more or less definite period. Okuma also noted after transplantation that the sebaceous glands at first atrophy but later tend to resume their function and recover their normal shape.

The experiments reviewed were conducted on animals and dealt with the production of an epidermal cyst by transplantation of epidermis into other tissues and with the production of a cyst from hair follicles when a section of skin of full thickness was implanted or when a foreign body was introduced into the dermis.

In a recent experiment, Paddock and I¹⁴ buried free sections of human abdominal skin from which the epidermis had apparently been removed and excised the grafts for histologic examination at intervals varying from seven days to twelve months. Small portions of the epidermis persisted in spite of attempts at complete removal. This epidermis formed small cystic cavities in the sections up to two months but did not appear in later sections. In the seven and twelve month sections there were small cystic cavities containing horny material but with a complete absence of epithelial lining. Other striking features in the sections were the early complete disappearance of the sebaceous glands and hair follicles, with persistence of sweat glands in all of the buried grafts.

The following work was done as a continuation of these experiments, to confirm the disappearance of the epidermis in buried human skin.

11 Imakita, T. Beiträge zur Kenntnis der Implantation der Haut. Ueber die Implantation der Hautstücke in das Muskelgewebe, *Acta dermat* **20** 137, 1932.

12 Imakita, T. Beiträge zur Kenntnis der Implantation des Hautgewebes. Ueber die Bedeutung der Mitosezahl an den Epithelzellen des implantierten Hautgewebes, *Acta dermat* **20** 138, 1932.

13 Okuma, M. Experimentelle Studien über den Entstehungsmechanismus der Epithelzyste. I. Ueber das Verhalten eines subkutan autoimplantierten Hautstückchens, *Nagasaki Igakkwai Zasshi* **14** 94, 1936.

14 Peer, L. A., and Paddock, R. Histologic Studies on the Fate of Deeply Implanted Dermal Grafts. Observations on Sections of Implants Buried from One Week to One Year, *Arch Surg* **34** 268 (Feb.) 1937.

EXPERIMENTAL PROCEDURE

A free elliptic section of skin and subcutaneous fat was removed from the chests of a number of patients on whom a rib graft operation was to be performed for the repair of saddle nose. The free section of skin and fat was transplanted with the hoarded excess of rib cartilage beneath the skin of the chest (fig 1). After successful repair of the saddle nose the hoarded rib cartilage was removed from the chest, together with the buried segment of thoracic skin. The cartilage was then removed from the excised tissue and

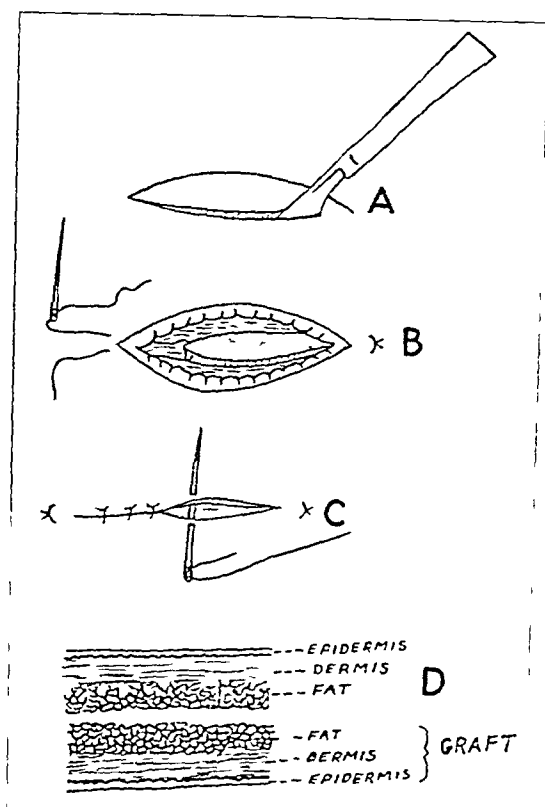


Fig 1—Diagrams showing how the skin and fat grafts were transplanted. *A*, elliptic section of skin and fat excised from the chest wall. *B*, section of skin and fat inserted in the wound with the cutaneous surface down and the fat surface outermost. Mattress sutures through the ends of the graft hold it in position. *C*, subcutaneous fat and skin sutured to cover the graft. *D*, cross section of the area of transplantation showing the relation of the graft to the overlying skin of the chest.

the portion containing the buried skin graft was fixed in Zenker's solution. After sectioning in the usual manner the tissues were stained with hematoxylin and eosin and after examination they were photographed under high and low power magnification.

had migrated from the host tissue and appeared to be attacking the epidermal layer of the graft. The epidermis of the graft was thinner than normal in the depths of indentations and in places was separated from the underlying dermis. A higher power magnification showed spaces scattered through the deep layer of the transplanted epidermis which were interpreted as representing degenerative change. The space between the epidermis of the graft and the host tissue was occupied by extruded horny material, fragments of hair from the epidermis and giant cells from the host tissue containing partially digested fragments. The free ends of the epidermis did not appear to be growing in the form of a horseshoe as reported by experimenters with animals, and

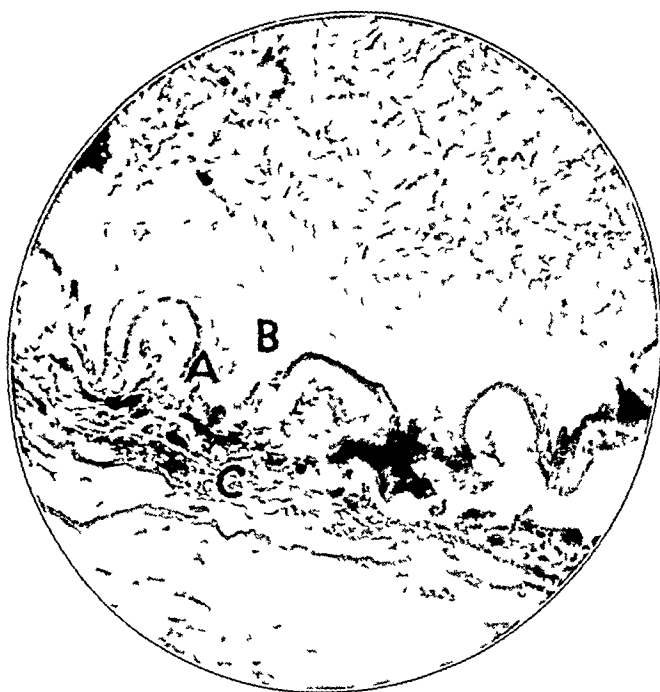


Fig 5—Section of the transplant at one month, showing, the epidermis of the graft (A), the dermis of the graft (B) and the host granulation tissue rich in giant cells (C). The epidermis is thin in the depths of the indentations and thicker at the tops of the papillae. The spaces between the papillae are occupied by giant cells and broken-down cornified material and fragments of hair.

the appearance as a whole suggested degeneration and partial absorption of the epidermis. Numerous hair follicles and sweat glands were seen in the dermis of the graft, but no sebaceous glands were seen. On the basis of the absence of sebaceous glands in all of the later sections I concluded that they had entirely degenerated between two and four weeks after transplantation.

A careful study of the sections buried for ten weeks showed no surviving epidermis. The granulation tissue of the host was in close

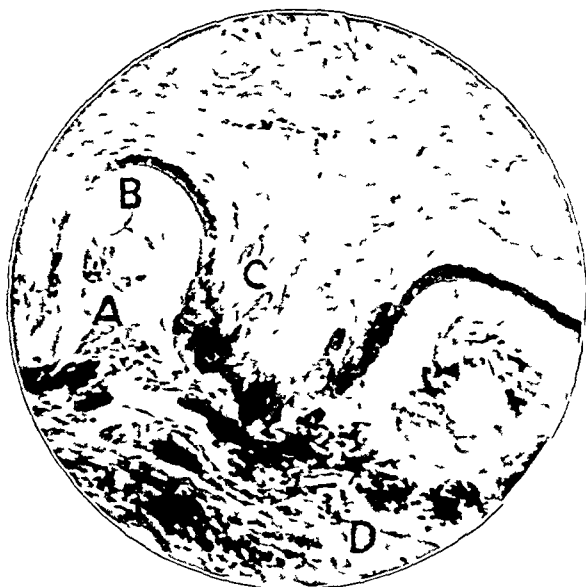


Fig 6—Section of the transplant at one month (high power magnification) In the space between the papillae are shown a group of giant cells (*A*) and broken-down cornified material (*B*) At *C* processes from the epidermis of the graft appear to penetrate into the dermis *D*, host tissue



Fig 7—Section of the trans-plant at one month (highest power magnification) showing in detail the host granulation tissue (*A*) in relation to the epidermis of the graft (*B*) Note the group of giant cells (*C*) between the granulation tissue of the host and the epidermis of the graft Numerous spaces containing clear fluid are present in the epidermis of the graft at *D*

contact everywhere with the graft. Numerous collections of giant cells were present on the under surface of the graft, where the epidermis had been present at the time of transplantation. Many of these giant cells contained refractile substances which may have represented bits of partially digested epithelium or fragments of hair. A few hair follicles and numerous sweat glands were seen in the sections. The sweat glands were approximately normal in appearance, but the hair follicles showed degenerative changes and were frequently seen in the midst of a cluster of giant cells. No sebaceous glands were seen in the sections.

The sections buried five and one-half months showed no surviving epidermis or sebaceous glands. Numerous sweat glands were present



Fig 8—Section of the transplant at ten weeks, showing the approximately normal appearance of the sweat gland tubules in the dermis of the graft

in the dermis of the graft, but only one hair follicle was observed. The graft was intimately fused with the surrounding host tissue, and there was no cellular activity about the surviving sweat glands.

The sections buried sixteen months showed the graft in close apposition with the surrounding host tissue. The region of the graft, indeed, could be located only by the presence of sweat glands in a fibrous tissue stroma located beneath the subcutaneous fat of the overlying thoracic skin. The sections showed no surviving sebaceous glands, hair follicles, or epidermis. The surviving sweat glands were approximately normal in appearance and showed no evidence of cyst formation.



Fig 9—Section of the transplant at ten weeks showing a giant cell (A) containing a retractor particle (B) believed to be a partially digested remnant of the epidermis of the graft

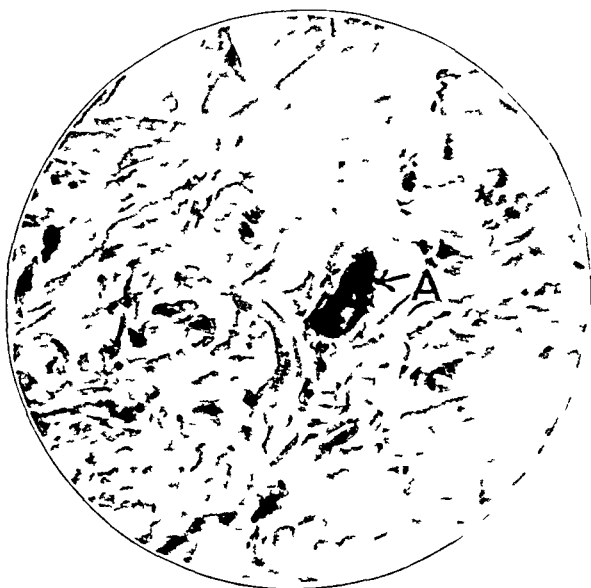


Fig 10—Section of the transplant at five and one-half months showing a surviving hair follicle (A) in the dermis of the graft. No remnant of epidermis or sebaceous glands were observed. Sweat glands were present in many of the sections.



Fig 11—Section of the transplant at sixteen months, showing surviving tubules of sweat glands in the dermis of the graft. No epidermis, hair follicles or sebaceous glands were observed.

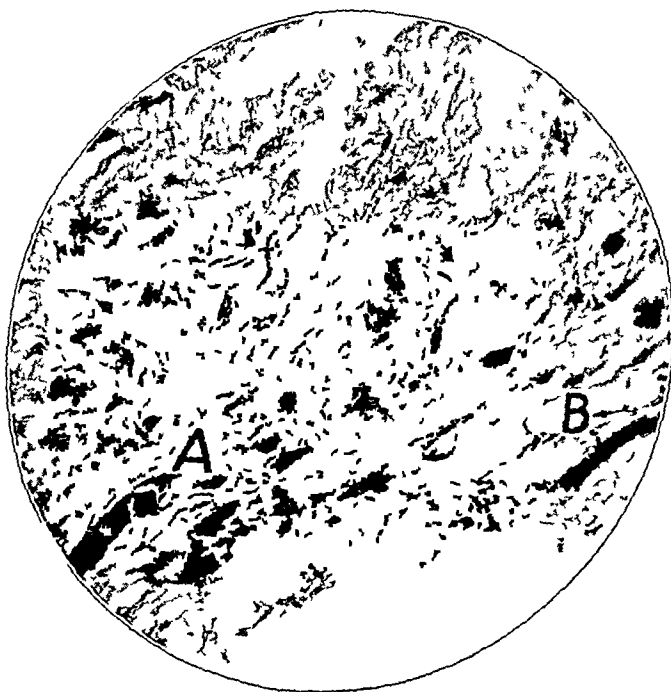


Fig 12—Section of the transplant at twenty-eight months, showing surviving tubules of sweat glands (*A* and *B*). The cells are darkly stained and the lumens extremely small.

The sections buried twenty-eight months showed the graft in close apposition with the surrounding host tissue. There were no surviving epidermis, sebaceous glands or hair follicles in the graft. Sweat glands were present but they were altered in form with greatly flattened epithelium. There was entire absence of cellular activity about the surviving sweat glands and no cyst formation was present. Refractile fragments were present in the buried dermis which were interpreted as remnants of broken-down hairs.

COMMENT

Comparison of my observations in sections of buried human skin with those of investigators working with buried animal skin shows a rather startling contrast. The epidermis of the human graft shows definite degenerative changes at one month and is entirely absent ten weeks after transplantation. The epidermis of animal grafts turns on itself in the shape of a horseshoe and when the two ends meet forms a closed cyst cavity which progressively increases in size. Zimches studied his grafts in dogs for periods up to two years and found the epidermal lining of the cysts still viable and the cysts themselves increasing in size. Sebaceous glands in buried grafts of human skin have completely disappeared one month after transplantation. Investigators working with animals have reported their survival for much longer periods. Hair follicles in buried human skin were not found after five and one-half months and did not tend to form cysts in the earlier sections. In animals cysts frequently have been reported as originating from the hair follicles. The sweat glands persisted in all of the buried grafts of human skin but did not lead to cyst formation in any of my sections. The fate of the sweat glands in buried grafts of animal skin was not described because the skin selected for burial did not contain sweat glands.

One may conclude therefore that in the human being buried thoracic skin of full thickness does not lead to cyst formation from the epidermis or from hair follicles, sebaceous glands or sweat glands in the buried section of skin.

In a previous experiment in association with Paddock I¹¹ buried small bits of abdominal epidermis attached to the dermis beneath the skin of the chests of human beings. Small cysts developed from the buried epidermis and persisted up to two months after transplantation. In later grafts buried seven months and twelve months small cystic cavities were found filled with epithelial debris but with complete absence of epithelial lining. It seems apparent that small bits of epidermis produce less reaction in the surrounding host tissue and survive long enough to form small cystic cavities. Eventually, however, the epidermis is completely absorbed.

On the basis of my findings in these experiments with buried human skin, I believe that the implantation theory of cyst formation in the human being is extremely doubtful. One must qualify this statement by assuming that the skin of the palm and fingers acts in the same way after burial as the skin of the chest and abdomen. There is also the possibility that autogenous buried skin in a few persons stimulates less reaction in the host tissue surrounding it and is able to survive and grow into a cyst. The most valuable information obtained from the experiments was the fact that autogenous skin buried in human beings acts differently from autogenous skin buried in animals (guinea pig, dog and rabbit).

SUMMARY

Six grafts of autogenous thoracic skin of full thickness were transplanted with the subcutaneous fat, beneath the thoracic skin of 6 human beings and removed at intervals varying from two weeks to twenty-eight months.

A microscopic study of sections of these grafts showed that the epidermis survived in the two week graft and in the one month graft but was entirely absent in all of the later grafts.

The sebaceous glands were present in the two week sections but showed definite degenerative changes. No sebaceous glands were observed in any of the later sections.

Hair follicles were observed in all of the sections up to and including those examined at five and one-half months. They were absent in those examined later.

Sweat glands were observed in all of the sections up to and including those examined at twenty-eight months.

Neither cyst formation nor malignant change was observed in any of the sections.

Autogenous full thickness skin buried in the human being acts differently from autogenous full thickness skin buried in animals (dogs).

On the basis of the findings in these and previous experiments with buried human skin, I believe that the implantation theory of cyst formation in man is doubtful.

The sections described in this paper were prepared by Mr. David J. McKinnon of the Newark Eye and Ear Infirmary. Dr. Royce Paddock aided in interpretation of the microscopic observations.

REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomaly—Braasch¹ reviewed the urographic and clinical data in 102 cases of renal fusion observed at the Mayo Clinic from 1930 to 1938. The terms in current use such as 'horseshoe kidney', 'lump kidney', 'sigmoid kidney' and "crossed renal ectopic" are confusing and should be discarded in favor of a more accurate designation based on the relation of the fused kidneys to the vertebral column. Thus renal fusion is bilateral when the two renal pelves are situated on opposite sides of the vertebral column, prevertebral when one or both pelves are situated anterior to the midvertebral line and unilateral when both pelves are situated on the same side. Bilateral fusion was observed in 84 cases, unilateral fusion in 13 and prevertebral fusion in 5.

Renal fusion may be inferred in about half the cases from changes in the renal outlines as seen in plain roentgenograms. Stones are a frequent complication (they are observed in 25 per cent of cases of bilateral fusion) and their position aids in the recognition of the anomaly. When the stone is large and partially fills the renal pelvis the cast of the stone will have a deformity similar to that of the shadow observed in a urogram.

¹ Braasch W F and Hammer H J. Renal Fusion. Urographic Data and Their Clinical Significance. Brit J Urol **10** 219-230 (Sept) 1938.

The following urographic data are of importance in the recognition of bilateral fusion

1 In 60 per cent of cases one or both renal pelves are below the third lumbar vertebra

2 In the majority of cases the right pelvis is higher and closer to the vertebral column than is the left pelvis

3 The calices extend in a direction reversed from the normal, and the most significant diagnostic factor is the characteristic axis of the lower calyx which is directed downward and inward toward the isthmus and may overlap the vertebral column. Occasionally the lower calices of the two pelves are so closely related that surgical separation of the respective renal segments is difficult or impossible. This is true especially in cases of unilateral fusion

4 The point of insertion of the ureter into the pelvis is frequently lateral or anterolateral instead of mesial

Although the pelves are situated closer together than is normal, their wide separation does not preclude the possibility of fusion, and although fixation of the renal mass is usual, ptosis of one or both segments can occur and can be demonstrated urographically

Pyelectasis, caliectasis and ureterectasis occur in 81 per cent of cases of fused kidneys. In some instances the dilatation is not associated with pain or obstruction and is considered a congenital abnormality associated with the anomaly and not a pathologic complication. In other instances the pyelectasis is acquired and is associated with stasis. This point should be checked by delayed retrograde urographic study, for the pain and infection associated with stasis can be relieved in some instances by separation of the two renal segments with nephrolysis and nephropexy

Torre² had occasion to do a heminephrectomy on a man 33 years of age with horseshoe kidney complicated by stone andiliary abscesses. The clinical and pyelographic diagnosis, made preoperatively, was renal lithiasis with ureteral obstruction and acute pyelonephritis on the left in a horseshoe kidney. The two kidneys were united at the lower poles. The operation was followed by uneventful recovery. The horseshoe organ had given no symptoms until the stone developed. Apostematous nephritis in a horseshoe kidney is a condition rarely encountered. The good visual exposure given by the reflector made it possible to recognize easily the line of demarcation between the two kidneys and indicated where the section should be made.

With the means available today to the urologist, the diagnosis of horseshoe kidney has become relatively easy. It remains true, however

² Torre, D. Nefriti apostematosa litiasica sur rene a ferro di cavallo, *Arch ital di urol* **15** 15-32 (Jan) 1938

that "to make the diagnosis, one must think of its possibility," and it is evident that the surgeon does not always think of it. Only with the more extensive use of descending urographic examination will the percentage of preoperative diagnoses increase.

In 169 cases collected by Schilling lithiasis was present 69 times, hydronephrosis 35 times and tuberculosis 24 times. Tumors have been reported in 13 instances, pyonephrosis in 9 and cysts in 5. A horseshoe kidney may have any of the diseases which attack a normal kidney. Bottez found 16 per cent of such kidneys diseased. Bayer set the percentage at 39 and others have placed it still higher.

Horseshoe kidney demands a proper operative technic in relation to its modified anatomic position with ptosis and rotation, its median position, the almost constant presence of anomalous vessels, the existence of an isthmus and the fixity of the organ. Nephropexy alone does not improve the symptoms that accompany horseshoe kidney, since the low insertion of the vascular pedicle, the anomalous vessels and (frequently) short ureters hinder such reposition. Nephropexy combined with section of the isthmus, however, is a logical procedure. When lithiasis is present, as in the case reported by Torie, pyelotomy must be done *in situ* since the organ cannot be exteriorized. Nephrectomy is the operation most frequently done, either because the kidney, owing to its anatomic position, is more subject to destructive lesions or because the surgeon, facing a doubtful outcome, decides promptly on removal rather than on doing an operation in two stages with the difficulties this would make later. The difficulties of nephrectomy consist in the presence of anomalies of vascularization and in the fact that the isthmus holds the kidneys in a median position that makes exteriorization impossible.

Before section of the isthmus the surgeon must determine whether there are any arteries in the isthmus, must find the exact limits of the two components of the horseshoe mass and must determine whether the ureter of the opposite side runs within the isthmus. It is also important not to leave within the wound a fragment of the removed kidney in which the excretory passages would be suppressed and not to suppress by a too comprehensive incision a calyx of the opposite kidney. In either instance a fistula would result. One must make sure that ligation of the isthmus does not obstruct the course of the ureter of the opposite side.

Wilmer³ reported 5 cases of unilateral fused kidney together with a series of 94 cases collected from the literature. In about 60 per cent of the cases the kidneys were found on the right side. The anomaly appears to be equally distributed between the sexes. In the great majority of cases in which the condition was detected either clinically

3 Wilmer H. A. Unilateral Fused Kidney. A Report of Five Cases and a Review of the Literature. *J. Urol.* 40: 551-571 (Nov.) 1938.

or at necropsy the patients were less than 50 years of age. Unilateral fused kidneys seem predisposed to hydronephrosis and pyelonephritis but not to other renal lesions. This anomaly falls into six classes: (1) elongated kidney, (2) S-shaped kidney, (3) L-shaped kidney, (4) mesial fusion, (5) lump kidney and (6) "superior kidney ectopic." The unilateral fused kidney is seen about once in 7,500 autopsies. Fusion of the kidneys is facilitated by a mechanical obstruction at the bifurcation of the aorta into umbilical arteries. These vessels form a crotch which may force together the ascending blastemas. Great variation exists in position, rotation and vascular supply of the unilateral fused kidney. The most common symptom is pain. The renal mass is usually palpable, especially if it is involved in a lesion. Frequently there are urinary symptoms. The diagnosis can be easily and accurately made by taking a pyelogram, which will show the ureter of the ectopic kidney crossing the midline to terminate normally in the bladder, presenting a "triangle" pyelogram.

Beer and Mencher⁴ reported a series of 104 cases of double kidney from the records of the Mount Sinai Hospital. Of the 104 cases, there were 89 of unilateral double kidney (85.5 per cent) and 15 of bilateral double kidney (14.5 per cent).

In 14 cases a heminephrectomy was done, with a single operative mortality. The disease was limited to the upper pole in 4 cases (28 per cent); of the 4 patients, 2 had ectopic ureters. The upper pole and its ureter were removed, the lower half of the kidney being preserved. In 10 cases the lower pole showed involvement, and in these the lower half was removed, the upper portion being allowed to remain. The lesion in 6 cases was pyonephrosis, in 5 cases, hydronephrosis, in 1 case, calculous hydronephrosis, and in 2 cases, multiple calculi. In none of the cases was it necessary to perform a secondary removal of the residual portion.

Stone calculated that in 10 per cent of a series of 30 collected cases secondary nephrectomy was required. It is of interest to note that in 12 of the 42 cases of nephrectomy reviewed by Eisendrath there was no abnormality in one segment, in other words, heminephrectomy would have been the more conservative procedure. In 5 additional cases in his series, technical difficulties prevented a heminephrectomy, and a complete nephrectomy was performed.

In all cases which were followed up by cystoscopic or pyelographic study, good function of the remaining portion of kidney was shown at variable lengths of time after the operation.

It is evident, therefore, from a study of Beer and Mencher's cases that conservatism is most important and that renal tissue should be

⁴ Beer, E., and Mencher, W. H. Heminephrectomy in Disease of the Double Kidney. Report of Fourteen Cases, *Ann Surg* 108:705-729 (Oct.) 1934.

saved whenever possible. This point may be emphasized by reference to a patient who has been living for eleven years with approximately one sixth of the normal amount of renal parenchyma.

Deming⁵ stated that the expectancy of life of the unilaterally nephrectomized person depends on (1) the cause for which the kidney was removed, (2) the condition of the remaining kidney and (3) the social status of the patient. Certain operative procedures applicable to tuberculous and pyogenic conditions are available which diminish the mortality and shorten the postoperative course. The young person whose kidney has been removed for causes other than malignant tumor has a normal expectancy of life. Marriage is permissible for persons who have a normally functioning kidney a reasonable length of time after nephrectomy. Pregnancy is permitted for all healthy women who have not had a malignant lesion.

Tumor—Kerr⁶ reported 14 cases of renal neoplasm in children treated by irradiation with roentgen rays followed by operation. Two patients are still alive and without evidence of disease fifty-nine and fifty-two months respectively after admission to the hospital. One had previously been shown to have pulmonary metastasis. Operation should not be deferred beyond the time of continued regression of the tumor. It is worth while to irradiate metastatic lesions and local recurrent lesions intensively.

Hyman and Wilhelm⁷ discussed the differential diagnosis of renal and suprarenal tumors. They stated that tumors of the upper pole of the kidney and in the suprarenal region may for practical purposes be considered under the following headings:

- 1 Cyst
- 2 Inflammatory exudate or abscess
- 3 Neoplasm of the upper pole of the kidney
- 4 Neoplasm in the suprarenal region
 - (a) arising from the adrenal gland
 - (b) not arising from the adrenal gland
- 5 Splenic enlargement

Tumors arising in the suprarenal region when they attain a large size dislocate the kidney but do not usually distort or obliterate the upper calices. Intrinsic renal tumors on the other hand often encroach

5 Deming C L. The Future of the Unilaterally Nephrectomized Patient. *Tr Southeast Br Am Urol A* Nov 5 1937 pp 2-10

6 Kerr, H D. Treatment of Malignant Tumors of the Kidney in Children. *I A M A* **112** 408-411 (Feb 4) 1939

7 Hyman A and Wilhelm S F. The Differential Diagnosis of Renal and Suprarenal Tumors. *I Urol* **40** 737-751 (Dec) 1938

on the outline of the renal pelvis and calices. Blood in the urine also points to intrinsic renal tumor.

Intravenous and retrograde pyelographic procedures are of great value in demonstrating renal and suprarenal tumors. Minimal pyelographic changes, such as the flattening or absence of a minor calix, may be the sole sign of a large tumor. Displacement of the kidney, especially on the left side, is significant.

Perirenal insufflation is of limited value. A case of collapse following its use was reported. The authors stated that this method should be employed with great caution.

The degree of renal mobility is determined by taking roentgenograms with the patient in the Trendelenburg and in the "reverse Trendelenburg" position. Fixation of the kidney has been found in cases of perinephritis and of infiltrating carcinoma.

Lucke⁸ stated that the leopard frog is commonly affected with adenocarcinoma of the kidney. As in the case of mammalian neoplasms, this tumor remains localized when small and in its early stages, but when large it frequently forms secondary tumors in distant organs. Dissemination usually takes place by way of the blood stream. Lucke reported 22 new examples of metastasis. His observations of frequent metastasis make the evidence for the malignancy of this tumor complete.

Infections—Ball⁹ stated that infections of the kidney by staphylococci are relatively rarely seen. They usually involve the cortex, are hematogenous and are commonly secondary to suppurations in the skin.

Three types of lesions are recognized. Lesions of the first type, multiple minute abscesses studded throughout the renal cortex, are seen in cases of severe acute pyemia associated with such diseases as acute osteomyelitis type. The second type, a superficial triangular septic infarct just under the renal capsule, is probably present and seldom seen in patients in whom a perinephric abscess heals after adequate drainage has been instituted. The third type is the lesion commonly found deep in the cortex and known as "renal carbuncle," which results in formation of a persistent fistula after drainage of the perinephric abscess and which will not heal until the kidney is removed or if it heals will be followed by a recurrence of symptoms.

In all attempts to reproduce these lesions experimentally, intravenous injections of cultures of *Staphylococcus aureus* in varying doses were made in rabbits. The animals were killed at the end of varying periods up to two weeks. It was learned that lesions similar to those found in man can be produced in the rabbit, that the abscesses formed

⁸ Lucke, B. Carcinoma of the Kidney in the Leopard Frog. The Occurrence and Significance of Metastasis, *Am J Cancer* **34** 15-30 (Sept.) 1938.

⁹ Ball, G. Staphylococcal Infections of the Kidney, *Brit J Urol* **10** 323 336 (Dec.) 1938.

by the introduction of staphylococci into the blood stream are more likely to form in the kidney than in other organs, that they are slow in their formation, that both superficial and deep lesions are formed, the latter, resembling the "renal carbuncle" of man, being slowest in their formation and that the resistance of the animal determines the number and rapidity of development of the lesions. It was disappointing that a perinephric abscess did not form in any of the animals as it was hoped to demonstrate its relation to a superficial renal infarct.

The disease occurs more often in men than in women. There may be a period of two to eight weeks, sometimes much longer, after the cutaneous lesion occurs before there is evidence of general infection. General infection is characterized by malaise, fever, rapid pulse and leukocytosis without localizing symptoms either in the kidneys or in other organs. These symptoms may become chronic and may continue for a long period before there is any clue to their origin. The length of this period depends on the depth of the lesion from the surface of the kidney. The urine may be normal even in advanced stages except for a few leukocytes, erythrocytes, a trace of albumin or a few staphylococci observed after centrifugation.

Ball reported 5 cases of renal carbuncle and concluded that in arriving at a diagnosis these points should be kept in mind: 1. There is a history of a primary staphylococcic lesion which may be present at the time of formation of the renal focus or may have healed months before. 2. In the early stages, absence of symptoms relating to the urinary tract is a common feature. 3. There is invariably a high leukocyte count. 4. When the condition is suspected, pyelographic procedures may be a most useful method of investigation in arriving at an early diagnosis of the renal lesion. If intravenous pyelographic procedures are used, it is possible that the dye may fail to show in the affected kidney; should this occur or should the diagnosis still be doubtful, there should be no hesitancy in resorting to the retrograde method. Widening or obliteration of the calices is the picture commonly obtained. With the superficial renal lesion it is possible that no defect may be found, but if the lesion is large or is of the deep variety, this method of diagnosis is invaluable. 5. At a later stage when there are obvious physical signs in relation to the kidney, as a rule a perinephric abscess has already formed. It is worth while to obtain a pyelogram even at this stage as an indicator for subsequent treatment. 6. If there is still doubt, the loin should be explored surgically.

Treatment should be as conservative as possible. Drainage of a perinephric abscess may suffice. The change in the pyelograms and the clinical progress will determine whether a subsequent early nephrectomy is indicated.

If a perinephritic abscess is not found, pyelographic examination will determine whether early removal is indicated and whether a prolonged illness can thereby be prevented.

Ryle¹⁰ divided staphylococcic perinephritis into two types, the septicemic and the nonsepticemic. In the former the toxic symptoms overshadow the local signs of perinephritis. In the latter a renal abscess is the only metastatic focus to be discovered, the onset is insidious, and the symptoms are not severe.

Ryle said that staphylococcic perinephritis complicating a renal carbuncle is a disease of early or middle adult life and is rare in childhood. All of his patients were males, and their ages varied from 9 to 45 years.

In 9 of the 11 cases the etiologic factor was a cutaneous boil or carbuncle. The interval between the primary infection and the occurrence of a renal metastatic lesion varies from two weeks to two months, although the staphylococcus may be dormant for years.

With staphylococcic septicemia the prognosis is poor. Of Ryle's 13 patients, 7 (54 per cent) died, 3 of the 13 patients had renal foci with perinephritis, and only 1 of these 3 recovered.

In the nonsepticemic group the 8 patients who had perinephritis all recovered, 6 of them after simple drainage and 2 without surgical intervention.

Treatment generally should be conservative.

Dukes¹¹ said that the finding of staphylococci in the urine when contamination and faulty collection have been ruled out is an important observation because infection of the various parts of the genitourinary tract with these organisms has distinct clinical significance.

The characteristic lesion in the kidney is cortical suppuration or carbuncle. The infection is embolic from abscesses elsewhere or from the upper portion of the respiratory tract and the suppuration may spread to the perinephric space or pus may discharge into the pelvis.

In the early stages the urine does not contain pus, but the centrifuged specimen may show a few clumps of gram-positive cocci and cultures may show a growth of *Staph aureus*. Secondary infection with *Bacillus coli* occurs in about half the cases and tends to persist longer than the primary infection.

Surgical treatment is necessary in many cases, but mild infections may disappear spontaneously or may respond to medical treatment.

Staphylococcic infection of the bladder is uncommon except after instrumentation or in the presence of obstructions, diverticula, malignant

¹⁰ Ryle, J. A. Perinephritis, *Brit J Urol* **10** 337-347 (Dec.) 1938.

¹¹ Dukes, C. E. The Clinical Pathology of Staphylococcal Infections of the Urinary Tract, *Brit J Urol* **10** 373-378 (Dec.) 1938.

growths or calculi. It may be the cause of cystitis with alkaline incrustation and a factor in the formation of stone.

Staphylococcal urethritis and prostatitis frequently follow gonorrheal infections or they may be primary infections and may be transmitted by sexual intercourse. Extension to the epididymis is not uncommon, with formation of an abscess which involves the testicle.

Some strains of staphylococci are capable of splitting urea with the formation of alkaline urine. When obstruction and stasis are present with these infections stones composed of the earthy phosphates are likely to be formed with staphylococci as nuclei. The term staphylococci can be applied to many of these urea-splitting gram-positive diplococci only in a general way.

The mixed character of these urinary cocci is shown by the work of Stadnichenko,¹² who studied thirty strains of gram-positive cocci isolated in cases of genitourinary infection and found fourteen strains which decomposed urea. Eight of these produced an orange-colored growth on agar, and six showed a white growth. No cultural characteristics other than fermentation of dextrose and sucrose were common to these fourteen strains.

Dukes said that the question whether staphylococci in the urine are of pathologic significance can be decided generally by the patient's clinical condition, the manner of collection of the specimen and other findings in the urine. *Staph. aureus* is usually pathogenic with albus strains. The following points may help to determine whether the organism is contaminated or of clinical significance although only in exceptional cases is it worth while to make such a determination:

1. Hemolytic staphylococci are more likely to be pathogenic than nonhemolytic strains although this cannot be accepted as an invariable rule.

2. Staphylococci which rapidly liquefy gelatin are more likely to be pathogenic than nonliquefying strains.

3. Some strains of staphylococci secrete a ferment known as coagulase. The presence of this ferment can be shown by adding a small quantity of a culture to oxalated rabbit plasma and incubating the mixture at 37 C for three hours. The occurrence of coagulation is to be taken as evidence of pathogenicity in the strain tested.

4. Toxic substances may be shown to be present in filtrates of broth cultures of some strains of staphylococci. When injected into the peritoneal cavities of laboratory animals these toxic substances excite peritonitis and under the skin they give rise to cellular infiltration and to formation of an abscess. Virulent staphylococci are likely to produce more of this substance than nonvirulent ones.

12 Stadnichenko, A. M. S. Thirty Strains of Gram-Positive Cocci Isolated from Cases of Genito-Urinary Infections. *J. Bact.* **17**: 703 (May) 1929.

Renal Tuberculosis—A study was made by Emmett and Kibler¹³ of 1,131 consecutive patients on whom nephrectomy was performed for renal tuberculosis at the Mayo Clinic between 1912 and 1932. The purpose of the study was to determine, if possible, the prognosis after nephrectomy on the basis of observations obtained in clinical investigation of the so-called good kidney prior to operation. From this study it was hoped to be able to bring about a closer agreement among urologists as to the amount of clinical investigation necessary to determine the character of a "good" kidney before removal of the "bad" kidney is advised. The study showed the results from five to twenty years after nephrectomy. The patients were grouped according to the type of investigation carried out on the "good" kidney and also according to the findings obtained from such studies.

Seven tables indicated in detail the interesting results, which may be briefly summarized as follows. In order to make a fairly accurate prognosis catheterization of the good kidney to determine the amount of pus being secreted is imperative. The presence of normal urine leads to a favorable prognosis, and statistical data indicate that the patient may expect approximately a 43.5 per cent chance of a five year cure, a 65.2 per cent chance of being cured or improved in that period and only a 20.3 per cent chance of death within five years. If, in addition to this, inoculation of a guinea pig gives a negative result and a positive acid-fast stain is not obtained, the patient's chance of dying within five years will drop to 13.3 per cent, his chance of a five year cure will be increased to 50.3 per cent and his chance of being either cured or improved will increase to 75.2 per cent. On the other hand, if the results of inoculation of the guinea pig are positive, the patient's chance of dying within five years increases to 41.8 per cent and his chance of a five year cure drops to 21.8 per cent. These figures are dramatic and demonstrate that the results differ greatly in cases in which the urine from the good kidney is normal, depending on whether the results of inoculation of the guinea pig are positive or negative.

The question then arises. Should a positive result from a guinea pig test corresponding to the good kidney, in spite of absence of pus in the urine, be considered a contraindication to surgical operation? It must not be forgotten that 21.8 per cent of the patients were cured, that a total of 36.4 per cent were either cured or improved at the end of five years and that 30 per cent were either cured or improved at the end of ten years. Certainly almost any one who had the disease would be willing to submit to operation if given a 30 to 36.4 per cent chance of improvement for from five to ten years. If other factors do not consti-

¹³ Emmett, J. L., and Kibler, J. M. Renal Tuberculosis. Prognosis Following Nephrectomy, Based on Preoperative Observations in the 'Good' Kidney. J. A. M. A. **111** 2351-2356 (Dec. 24) 1938.

tute contraindications to surgical operation and if the excretory urogram of the good kidney is within normal limits, it seems that a positive result from a guinea pig test should by no means be considered a contraindication to surgical measures although it would considerably alter the prognosis. The common procedure, therefore of performing nephrectomy in such cases without awaiting the report of the results of inoculation of animals would appear to be justified.

When pus is found in the catheterized specimen of urine from the good kidney the problem is radically altered. Because of the small number of such cases in this series it is difficult to make as far-reaching statements as have been made concerning cases in which the urine was microscopically normal. However the study suggests that if more than 3 pus cells per high power microscopic field are found and if the guinea pig test or the stain gives a positive result, the prognosis is poor and it is questionable whether operation is warranted. In such cases no doubt fairly advanced bilateral renal tuberculosis is present and the possibility of clinical improvement or the better of the two kidneys after operation certainly is questionable. If there is a small amount of pus it inoculation tests and stains give negative results and if the excretory urogram is normal, the prognosis seems to be reasonably good and possibly surgical measures are worth a trial. This is true especially if there are not more than 10 or 15 pus cells per high power microscopic field in the centrifuged specimen of ureteral urine.

Perinephritic Abscess—Astral-di Fernandez and Brea¹⁴ reported a case of purulent perinephritic fistula which had been draining for five months when it came under their observation. The history given by the patient was as follows. Six or more months previously he had had an interdigital infection of the right hand which had to be opened surgically after symptoms had been present for two weeks. A week or so later he became feverish again and began to have persistent pain in the right lumbocostal region. Three weeks later his urine became purulent. For this he was subjected to a lumbotomy and an abscess was drained of a large amount of pus. A persistent discharging fistula remained which at length brought him to the authors' observation.

The first clinical impression was of a perirenal purulent fistula that might be due to a small abscess or to a foreign body (possibly an overlooked instrument) although the roentgenogram did not reveal any such objects. A sound was inserted in the fistulous tract and dissection was carried along its course which ran obliquely downward inward and backward. After resection of 6 to 8 cm. of the fistula it was found

14 Astraldi A. Fernandez I. S. and Brea L. M. Fistula purulenta lumbar. Osteitis vertebral no tuberculosis. Rev. argent. de urol. 7: 293-304 (Sep. Oct.) 1938.

to be oriented toward the vertebral column and not toward the perirenal capsule. A second study of the roentgenogram revealed osteitis of the third lumbar vertebra. The fistula was resected at this level and was drained and a suture was placed. Examination of the pus had revealed a pure culture of staphylococci. The fact that the lumbar or perirenal lesion had appeared during defervescence from a suppurative interdigital process seemed to point to a direct relation between the two conditions.

The rapidity with which the abscess had formed, one week after the infection of the finger and its roentgenologic character, showing osteitis of the pure vertebral type which affects the disks, supported the diagnosis of staphylococcal osteitis and excluded almost definitely the possibility of a tuberculous lesion with a preexistent ossifluent abscess flaring up as the result of a common interdigital infection.

The question arises: Was it this osteitis that secondarily brought about the formation of a perinephritic or pararenal abscess, which was primarily operated on? It seems difficult to doubt it. The vertebral osteitis and osteomyelitis, in an attempt to find drainage, gave rise to the perinephritic (or better, pararenal) abscess. To this the authors answer yes, because the dissection of the fistulous tract led directly to the vertebral region, without any view of the perirenal region during its course, and it was this fistulous tract that was drained in the first operation.

The condition in this case falls definitely into the category described by Tavernier in his discussion of the frequency of "false Pott's disease." According to him, the onset of these abscesses is sudden and febrile, the pain that accompanies them comes on with extreme rapidity, puncture affords no relief, but incision does, the fistula drains promptly unless a bony sequestrum maintains it, in which case the suppuration is more prolonged and refractory than in even the worst examples of true Pott's disease. The first three of Tavernier's requirements were fulfilled absolutely. As for the chronicity, which, according to Tavernier, would be interpreted as due to a sequestrum, the authors were unable to say whether one existed or not, since it was not looked for.

Hydronephrosis—Egger¹⁵ injected the arteries of hydronephrotic kidneys. Most of the specimens were from men with prostatic enlargement and obstruction, and Egger took roentgenograms of the visualized arterial system. The changes he observed explain how changes in the circulation affect the function of the hydronephrotic kidney. Back pressure destroyed the renal function, causing obliteration of the arterial interlobares by pressure and by dilatation of the calices, and thus created

15 Egger, K. Die Veränderungen des Nierenarteriensystems in der Hydronephrose und ihre Beziehungen zur Nierenfunktion, Ztschr f urol Chir u Gyn k 44 138-152 (July) 1938

ischemia of the renal parenchyma. The same mechanism causes an obstruction of the interlobar veins and venous stasis. This ischemia and venous stasis in connection with the increased pressure in the renal pelvis cause atrophy of the renal parenchyma. If the increased pressure of the renal pelvis is gradually reduced—for example, by emptying an overdistended bladder—the atrophied renal parenchyma may recover by an increased flow of blood. Sudden emptying on the contrary causes a large volume of blood to flow into the diseased arterial system under high pressure, reduces stasis and at times causes an even further reduction of renal function, sometimes resulting in death.

Cysts—Wehrbein¹⁶ reported a case of extravasation of urine due to rupture of a renal cyst with later encapsulation. He stated that in most cases perirenal extravasation is due to traumatic rupture of the kidney.

The case reported by him presented a different problem in diagnosis because the extravasation was atraumatic. The patient was a man aged 62 who had a sudden sharp pain in the region of the left kidney. He refused cystoscopic examination and a definite diagnosis was not made at the time of his first entry to the hospital. On his second entry there was still pain in the left renal region; he had lost weight and a soft mass was felt in the region of the left kidney. Cystoscopic examination revealed a continuous drip of urine from the left kidney such as occurs in cases of hydronephrosis. The kidney was explored and a large cyst apparently containing urine, was found. The kidney was pushed upward and the lower pole outward. The cyst and kidney were removed. Examination of the specimen showed a moderately hydronephrotic kidney with two intramural cysts which extended from the dilated middle calyx to the capsule. In the capsule a small hole was seen, through which urine had become extravasated into the perirenal fat. The wall of the extrarenal cyst was made up of fibrous tissue of inflammatory origin and did not show any epithelial lining. The fluid in the cyst contained 16 mg of urea per hundred cubic centimeters and was sterile.

Wehrbein assumed that the very thin wall of the cyst ruptured owing to some hydronephrotic distention and that urine became extravasated into the perirenal space causing pain, fever and peritoneal irritation with ileus. An inflammatory reaction resulted in walling off of the urine and with this the irritation of the peritoneum ceased and the ileus disappeared.

De Surra, Canard, Amestov and Bonfiglio¹⁷ on the basis of a case observed, discussed the anatomopathologic characters of pararenal serous cysts of which the most striking are those pointed out by Lecene and

16 Wehrbein H L. Urinary Extravasation Due to Rupture of a Renal Cyst with Subsequent Encapsulation. *Brooklyn Hosp J* 1:33-36 (Jan) 1939.

17 de Surra Canard R, Amestov J M and Bonfiglio O. Quiste seroso pararenal. *Rev Argent de urol* 7:317-324 (Sept-Oct) 1938.

Location. Such cysts are unilateral and of variable size and are included within the fatty capsule of the kidney, they are round, with a smooth surface and of a color related to the contents. The most common site of implantation is on the anterior aspect of the kidney. They become attached to the vascular pedicle and acquire a contact relation with the excretory passage. They develop downward, inward and forward, they form no adhesions to the peritoneum and are crossed by the colon.

The evolution of these cysts is silent, and their discovery is always accidental. The first symptoms are likely to be in the digestive system, on the same side as the cyst. Frequently constipation is the first sign. Usually there are few or no urinary symptoms, in some cases pollakiuria or hematuria appears early. Palpation of the abdomen reveals a tumor with retroperitoneal characteristics recognized as renal by its movement, which is synchronous with that of the kidney when there are no adhesions. One special peculiarity is the transverse movement that occurs on changes in the position of the patient, the cyst is felt under the examining hand and is due to the anterior implantation. Histologically it consists of endothelial cells, cuboid or flat, implanted on a fibrous capsule in which are elastic fibers and smooth muscle fibers.

Most writers agree that treatment should always be surgical, since, despite its benignity, the cyst is a progressive growth. Opinions differ, however, as to technic and the best mode of approach. While de Surra, Canard, Amestoy and Bonfiglio preferred the extraperitoneal route, their desire in this case to explore the abdominal cavity led them to make a transperitoneal approach with a transverse incision. Separating the ascending colon and the great omentum, they saw the tumor protruding behind the posterior leaf of the peritoneum, which they incised with care. Recognizing its cystic nature, they punctured it, since its removal whole would have required too great a breach in the peritoneum, its size being that of a fetal head at term. It was possible to free it on the anterior surface, but its close association with the region of the hilus in its implantation, with large vessels in intimate relation to the wall of the cyst, made its removal difficult, an attempt to section these vessels between ligatures revealed that their walls were too friable and that they tore in the grasp of the forceps. It was then decided to resect all of the cyst except this vascularized portion, which was left behind, at this level hemostasis was made by sutures, and the portion of cystic endothelium remaining in situ was touched with phenol to prevent recidivation. The postoperative course was uneventful, and the wound healed by first intention.

Only 5 other cases have been found in the literature in which the growth corresponded with the accepted description of a pararenal serous cyst. All the patients were women between the ages of 15 and 62 years.

Pyelonephritis—In reviewing 9 888 autopsies performed in the years 1931 to 1937 at Fahr's pathologic institute in Hamburg Hage¹⁸ found 598 cases of ascending nephritis and 69 cases of pyelonephritic contracted kidney. The incidence of contracted kidney was greater among women than among men, but that of pyelonephritis was about equal in the two sexes as well as the incidence on the right and the left side. In men pyelonephritis and pyelonephritic contracted kidney are more common in the later decades of life; in women they occur much earlier. In men the primary disease usually can be found, but not in women. Hypertrophy of the prostate gland is responsible for the frequency of pyelonephritis in old men, pregnancy accounts in a large number of cases for the occurrence of the condition in women. The mode of infection could be found in only a small number of cases. In cases in which the source of infection could be traced it usually ascended from the lower portion of the urinary tract. Hage stated that pyelonephritic contracted kidney is a very serious disease compared with atrophic glomerulonephritis and nephrosclerosis and that it is much more frequent than either. This is of great importance in the clinical evaluation of urinary infection.

Aneurysm—Kastner¹⁹ reported a case of aneurysm of the renal artery, of which he was able to find only 6 recorded cases in which the condition was diagnosed and treated. He reported the case of a woman 80 years of age who had hematuria of six months duration. She had recently had a severe hemorrhage which overdilated the bladder. The right kidney was found to be the source of the bleeding and nephrectomy was done. The kidney contained an old aneurysm (the size of an apple) of a branch of the renal artery, which was sclerotic. There was also a recent perforation of this aneurysm into the renal pelvis.

Renal Function—Gaudin and Cabot²⁰ stated that it has not been proved that damage to a kidney subsequent to obstruction is progressive and leads finally to death of the kidney. They concluded that the persistence of obstruction and the supervention of infection are of definite but unevaluated importance. They emphasized the fallacy of tests of renal function in the presence of obstructive lesions and again drew attention to the remarkable recovery of apparently functionless kidneys after surgical drainage. Three recent cases were presented which illustrated these points.

18 Hage W. Pathologisch-anatomische Statistik der Pyelonephritis und pyelonephritischen Schrumpfnieren. *Ztschr f urol Chir u Gynäk* **44** 172-181 (Juli) 1938.

19 Kastner, I. Nierenaneurysma. *Ztschr f Urol* **32** 442-444 (Juli) 1938.

20 Gaudin H. I. and Cabot H. The Reestablishment of Function in the Chronically Nonfunctioning Kidney Following Removal of Obstruction. *Proc. Staff Meet. Mayo Clin* **13** 388-391 (June 22) 1938.

In these cases although there was presumptive evidence of a kidney in which nonfunction had persisted for from six to ten years, prompt return of function followed surgical removal of the obstruction in each case. The authors pointed out that a functionless kidney does not of itself give rise to pain and that pain, when present, is evidence that the organ is capable of function. Decision concerning the advisability of nephrectomy must be made at the time of operation. In the case of stone in the middle or lower third of the ureter, it may be justifiable simply to remove the calculus without exploring the kidney, especially when there is a history of recent pain.

The authors stated the opinion that such conservative management will preserve many valuable kidneys which otherwise might be unnecessarily sacrificed.

Papillary Necrosis—Alken²¹ gave a description of what he considered a new pathologic entity, renal papillary necrosis. This condition usually occurs in diabetic persons with pyelonephritis. In some cases the kidneys show characteristic changes. Inflammatory processes localize at the base of the papilla, where a narrow zone of destruction occurs. The papilla then becomes necrotic, drops into the renal pelvis and may be passed through the ureter, causing hematuria and renal colic. The diagnosis is based on the fact that the patient has diabetes, there are urinary infection and the characteristic changes which occur in the roentgenograms and in the retrograde pyelograms. The condition is not uncommonly confused with early renal tuberculosis or an infiltrating neoplasm.

The small number of cases that Alken²¹ had observed did not permit him to generalize on the treatment. He stated that in his case therapy varied, but in some cases the condition is so severe that nephrectomy is necessary.

URETER

Stones—Alyea²² stated that the principles employed in cystoscopic removal of ureteral calculi are dilation, lubrication and anesthetization of the ureter and dislocation, grasping or crushing of the calculus.

It was suggested that complete relaxation of the ureter in its lower third is an aid in withdrawing large calculi. The most popular procedures are manipulations with catheters or bougies, spiral corkscrew stone dislodgers and cage-like instruments for grasping the calculus.

Calculi may remain in the lower third of the ureter for several years without causing serious damage to the upper portion of the tract. The calculi always have grooves in them or permit the urine to escape around them in some other way.

21 Alken, C. E. Die Papillennekrose, *Ztschr. f. Urol.* **32** 433-438 (July) 1933

22 Alyea, E. P. Cystoscopic Removal of Large Ureteral Calculi, *Tr. South. Urol. Br., Am. Urol. A.*, Nov. 5, 1937, pp. 11-28

A series of 327 cases of ureteral calculi is analyzed 72 per cent of the calculi were removed cystoscopically

Tumor—Hunner²³ reported a case of intussusception of the ureter in which the invagination was due to the drag of an unusually large papillomalike tumor Microscopically, this tumor proved to be a pure polyp, thus presenting a second extremely rare if not a unique feature From the history of intermittent attacks of moderate pain in the right flank for four years, Hunner concluded that the intussusception had been present for at least that length of time There had not been vesical symptoms suggestive of involvement of the urinary tract, and the results of urinalysis on many occasions had been normal except for the presence of albumin at the time when the patient was submitted to the first investigation of the urinary tract two years before operation The tumor plus the intussusception had led to astonishingly little damage to the kidney as was shown by the patient's good general health the differential functional test and study of the removed specimen

Hunner questioned whether the operation should not have consisted simply of excision of the tumor and reduction of the intussusception Had biopsy tissue been taken from the tip of the tumor projecting into the bladder, the simple morphologic structure of the tumor and Hunner's knowledge of the good functional capacity of the kidney undoubtedly would have led him to save the kidney

Foord and Ferrier²⁴ presented 6 proved cases and a probable seventh case of primary carcinoma of the ureter They collected a total of 139 cases, including their own

The basic triad of symptoms is hematuria pain and mass Hematuria was noted in 97, or 70 per cent of the 139 cases, in 11 there was no bleeding, and in 31 bleeding was not mentioned Pain is next in frequency It occurred in 84 (60 per cent) of the cases and was absent in only 11 The tumor palpated is nearly always the hydronephrotic kidney It is possible, however, for the kidney to be completely obstructed and not enlarged, as in Foord and Ferrier's first case It is rarely possible to palpate a tumor of the upper part of the ureter

On the plain roentgenogram an enlarged renal mass is often distinguishable Stones may occasionally appear coincidentally but they seem to have little etiologic significance

It is important that cystoscopic examination be done while bleeding is in progress, as a leading point is won by visualizing the bleeding meatus This was observed in 26 of 81 cases in which cystoscopic exam-

23 Hunner, G L Intussusception of the Ureter Due to a Large Papilloma Like Polypus *J Urol* 40 752-765 (Dec) 1938

24 Foord A G and Ferrier P A Primary Carcinoma of the Ureter with a Report of Seven Cases *J A M A* 112 590-601 (Feb 18) 1930

mation was performed. Tumor tissue was observed to project in 30 of 78 cases. The projecting tumor may so obscure the meatus that it is impossible to determine whether it originates in the ureter or at the edge of the meatus. A tumor may peep through the meatus only during ureteral peristalsis, or a telltale bulge may occur at that time. With a great proportion of ureteral tumors there is a complete block and no catheter or bougie will pass beyond the tumor. This was observed in 50 cases.

Excretory urograms usually show no dye in the affected side. They may faintly outline a hydronephrosis or, rarely, show a normal kidney on the affected side. The excretory urogram is inadequate to outline satisfactorily a ureteral filling defect.

In the cases so far reported the lower end of the ureter has been by far the commonest place for the tumor to appear, 85 of the tumors having been situated in the lower third, 23 in the middle third, 20 in the upper third, 6 in the entire ureter, 2 in the middle and lower thirds and 1 in the upper and middle thirds.

All authorities agree that the treatment of choice is early surgical extirpation, which means nephrectomy and ureterectomy. For 44 nephroureterectomies in one stage the mortality was 40 per cent, whereas for 22 nephroureterectomies in two stages the mortality was 5 per cent.

In a total compiled series of 100 operations, the mortality was 34 per cent at the end of three months. Scott, in 1934, in an effort to follow collected cases in which operation was performed, could find only 2 patients alive after five years.

Transplantations—Franché and Nguyen Trong-Hiep²⁵ presented the results of their experiments with implantation of the ureters into the rectum. Comparing these with the results of implantation into the bladder, they recorded as successful 25 to 30 per cent of implantations into the rectum, against 70 per cent of successes for the bladder. They accounted for the smaller number of the former by skeptic conditions in the rectal milieu, which undoubtedly plays an injurious role in cicatrization of the region of implantation. It was noted with reference to ureteropyelic peristalsis that, whereas all contemporary findings demonstrate that the ureter and pelvis respond to ascending infection with hypokinesia or akinesia, in the authors' experiments it was rather hyperkinesia that dominated in the group of failures, that is to say, the group in which implantation was followed by dilatation of the upper portion of the urinary tract.

Twenty-one experiments on dogs were reported and their results analyzed. In the first group (of 11 experiments) in which dilatation

²⁵ Franché, O., and Nguyen Trong-Hiep. *Recherches expérimentales sur l'implantation de l'uretère dans le rectum*, *J. d'urolog.* **46** 305-329 (Oct.) 1935.

occurred two important points were established 1 A correlation exists between ureteropyelic implantation into the rectum and an obstacle met by an exploring sound no 12 or no 14 2 This obstacle may appear as early as six or seven days after implantation The next 4 experiments were carried out to prove whether a mechanical obstacle might exist which the exploratory sound could overcome but which offered successful resistance to the wave of urinary fluid, that is, it was thought that a kink or a torsion alone or superimposed on a stricture might be the cause of the dilatation Experiments proved that this was the case In 1 of these 4 experiments the intestine was drawn out through a laparotomy incision and sectioned at a point just opposite the site of implantation The mouth of the ureter had assumed the appearance of a small caruncle In spite of the continuous action of ureteral peristalsis on its contents almost no urine entered the intestines Such urine as did enter the intestines did so at very wide intervals through the contracted orifice of an enormously dilated ureter behind which lay a voluminous hydronephrosis (forty-two days after implantation) By compression of the lower third of the ureter between the thumb and index finger a jet of urine was forced through which clearly revealed stenosis of the orifice A debridement of a few millimeters of this contracted orifice was all that was needed to cause a tremendous outflow of urine into the sigmoid portion of the intestine followed by ureteral contractions, which from that moment became effective and regular The peritonitis that followed caused the death of the animal so that it was impossible to carry out the intention of following the further course of this interesting experiment But it had already revealed dramatically the importance of the mechanical obstacle and also the long conservation of the dynamism of the implanted ureter, which far from having disappeared, had actually become exaggerated In a final group of 6 animals the results of implantation in the sigmoid portion of the intestine followed from seventeen days to six months were counted successful since there was no obstruction to the sound

A study of these results leads to the following conclusions 1 The dynamic ureteropyelic disturbance that sometimes follows section of the ureter is not definitive 2 Its persistence is due not to the traumatism itself but to its consequences namely stenosis of the ureter and (in 1 case) the irritative cicatricial 'epine'

While most experimenters have studied the dynamism of the ureters under direct examination alone these authors combined this with psychoscopic examination which in addition to giving admirable images has the advantage of presenting its views under almost physiologic conditions (without opening the abdomen)

BLADDER

Tumor —Grauer²⁶ reported a case of leiomyoma of the bladder in a woman aged 26, who complained of intermittent attacks of frequency, urgency and difficulty of passing urine. The onset had taken place two and one-half years previously, when the patient suddenly had acute retention of urine for twenty-four hours, requiring catheterization. Attacks of frequency of urination began regularly one week after menstruation and persisted until one week before the next menstrual period. The residual urine gradually increased to 350 or 400 cc.

Cystoscopic examination revealed pronounced coarse trabeculization of the wall of the bladder with deep pockets between the muscle bundles arising at the internal urethral orifice and extending intravesically so as to involve the left and anterior portion of the internal urethral orifice. There was a smooth, round lobe of firm tissue about 4 cm. in diameter, so situated that it obstructed the outflow of urine. The appearance "was not unlike that of a large left lateral lobe, prostatic hypertrophy." It was covered with normal vesical mucosa.

A suprapubic cystotomy and resection of the tumor was done.

The diagnosis was submucous leiomyoma of the neck of the urinary bladder.

Barringer²⁷ stated that three-year cures by radium in 215 cases of cancer of the bladder at Memorial Hospital occurred in 69 cases (32 per cent). Five year cures occurred in 52 cases (24.1 per cent), a drop of 76 per cent. The total number of cases in which the bladder became "cancer-free" was 96 (44.6 per cent).

The cancers in the cases were treated cystoscopically and by suprapubic implantation.

The authors included all cases, no matter how extensive the involvement, in which the bladder was opened. Radium was implanted in many extensive carcinomas "with the idea of controlling more cancers." Notwithstanding this effort, attempts to produce five year cures failed in about three fourths of all cases.

It is noteworthy that tumors of grade 4 have been controlled in only 2 cases. Barringer believed that with proper methods of irradiation carcinoma of grade 4 should not be more difficult to control than carcinoma of any other grade.

In most cases of fatal carcinoma death occurs within the first year. The chief cause of death is unquestionably severe infection of the bladder and kidneys. Probably few patients actually die of carcinoma.

²⁶ Grauer, T. P. Leiomyoma of the Bladder, *J. Urol.* **40**: 594-597 (Nov.) 1938.

²⁷ Barringer, B. S. Radium-Therapy of Bladder Carcinoma. Five Year Results, Failures, Future Therapy, *J. Urol.* **40**: 606-611 (Nov.) 1938.

The Carcinoma Registry has emphasized that vesical cancers are more often multiple than single. They have even seen fit to change the pathologic diagnosis from papilloma to carcinoma on the clinical basis that carcinomas are multiple. From the clinical standpoint, the fact that there are several tumors instead of one indicates in a broader sense that multiplicity of tumors constitutes a malignant element as compared with solitary tumors. On the other hand from Barringer's records carcinomas of the bladder are usually single.

The implantation of seeds into an infected tumor increases the severity of infection. A slough is always formed, and this presents a focus of increased infection. This slough may become incrustated with calcareous deposits and the formation of stone results. Asepsis and a certain amount of antisepsis help to obviate this condition.

Vesicovaginal fistulas may occur as the result of implantation of radon or the depth of the tumor or both. Barringer has observed 3 cases in which such fistulas were present.

Not only the size of the tumor but the infection of the tumor and the condition of the kidneys should determine whether suprapubic or cystoscopic treatment is to be used. Barringer stated that he leans more and more toward cystoscopic treatment. If the tumor is ulcerated and infected and if one or both of the kidneys are hydronephrotic, the suprapubic implantation of a large amount of radon is a dangerous procedure from the standpoint of the infection.

Incontinence—Gomez B²⁸ stated that during parturition the prolonged compression of the vesical neck and the urethra between the bony planes of the fetal head on the one hand and the os pubis on the other not infrequently results in injury to the sphincter of the vesical neck which under certain conditions produces incontinence. This may develop gradually during years or it may appear promptly after a brief period of retention owing to inflammation of the vesical neck and the urethra accompanied by paralysis of the bladder. Such retention may be total or partial. Distention residual urine and cystocele formation act progressively on the sphincter stretching its fibers until it finally becomes insufficient. In some cases insufficiency may result from the simple wounding of the sphincter without the presence of other complications. In any case the incontinence tends to be progressive until finally the loss of urine is constant whenever the patient assumes the upright position.

Treatment is surgical. Of the many procedures that have been tried the best is that of Marion. With the patient in the gynecologic position a Pezzer catheter is introduced into the urethra in such a way that its

²⁸ Gomez B. Carlos. Incontinence d'urine chez la femme par rétrécissement du sphincter vésical et son traitement. *J. urol.* 46: 344-356 (Oct.) 1915.

tip rests against the vesical neck, where it serves as a landmark at the moment of dissection. After suitable retraction of the vaginal walls and the labia minora a transverse incision is made in the vaginal mucosa, 3 to 4 cm. long, passing 2 or 3 mm. behind the meatus. The mucosa is grasped with a forceps and its dissection continued bluntly with a compress of gauze or with blunt-pointed scissors over an extent not less than 5 cm. until the entire region of the neck is uncovered. In dissection of the vaginal flap, the largest possible amount of muscular and fibrous tissue should be left to insure greater solidity.

Reconstruction of the vesical neck and the urethra is then begun, nonabsorbable sutures of linen or silk being used. With a Jalaguier needle a U suture is passed transversely in front of the urethra through the deepest part of the musculofibrous tissues which lie on each side of the midline. This is followed by two or three more sutures of the same kind, placed below the first in such a way that when they are tied they draw with them, under the vesical neck and the urethra, the lateral muscular and fibrous tissues. Emphasis is laid on the great care with which the first of these deep sutures must be placed, since if it perforates the vesical mucosa a vesicovaginal fistula is likely to result.

This done, the levator muscles on both sides are looked for and sutured in a second plane, transversely, with linen threads, as in an anterior colporrhaphy. Last of all, the vaginal mucosa is sutured at right angles to the other sutures, which it covers, this may be done with horsehair, agaffes or linen. With a tampon of iodoform gauze in the vagina, the operation is finished. This dressing is not removed until the fifth or sixth day, the patient being kept in complete immobility and in a state of constipation. Sutures are removed after nine or ten days. During all this time the catheter remains in the urethra, and care must be taken that it does not become clogged. After its removal on the twelfth day, the patient may not be able to urinate spontaneously for another week. In such cases (and these are among the best) catheterization should be done with a very small catheter. Eight cases are reported briefly.

Miller²⁹ stated that cystograms taken with the patient in the antero-posterior and oblique views in the dorsal, erect and erect straining positions yield information valuable in the selection of an operative procedure for repair of cystocele in individual cases. They are useful also in evaluation of the repair.

Urethrograms have proved an aid to investigation of the causes of incontinence and residual urine and have indicated the need, during repair, for special attention to narrowing the vesical neck and urethra.

²⁹ Miller, J. D. Studies on Cystocele and Urinary Incontinence in the Female by Use of Cystograms and Urethrograms, *J. Urol.* 40: 612-623 (Nov.) 1938.

correcting injuries to the trigonalis muscle and/or providing adequate fixation at the level of the internal sphincter

Day and Martin³⁰ stated that in practically every case of vesical diverticulum there is evidence of increased intravesical pressure over a long period almost always caused by obstruction at the outlet of the bladder

Of their 69 patients 42 had contracture of the vesical neck 25 had benign hypertrophy 1 had congenital valves in the posterior portion of the urethra and 1 had a filiform stricture in the urethra

In approximately 75 per cent of cases the orifice is situated from 1 to 3 cm above the interureteral ridge either mesial or lateral to the ureteral meatus

The sacs vary from pouches the size of a hazelnut to giant diverticula with a capacity of 2 liters or more Small diverticula are of little importance if the obstructing lesion is overcome, otherwise they grow although slowly

In contradistinction to the site of the orifice the direction of the protrusion varies The sacs may extend between the rectum and the bladder nearly as far as the subpubic ligament and in addition well up on the superior surface of the bladder

The first and fundamental consideration is surgical relief of the obstruction After this has been accomplished the diverticulum will seldom increase in size If the sac is not large empties fairly well and is not badly infected diverticulectomy is unnecessary in many instances On the other hand if the diverticulum is of the retention type or is large excision is indicated provided that the patient is a fair surgical risk

In many cases an operation in three stages is advisable that is preliminary cystostomy drainage should be performed with or without drainage of the diverticulum itself by means of an accessory Pezzer catheter introduced through the wall of the diverticulum In due course this should be followed by diverticulectomy and finally by surgical attack on the obstruction

Day and Martin³⁰ studied 69 cases of vesical diverticulosis in twenty-five years In 51 operation was performed for relief of obstruction at the vesical neck and in 32 diverticulectomy was performed Of the latter prostatectomy was done in 17 resecting of the vesical neck in 14 and electrodestruction of congenital valves in 10 There were 3 deaths and in 3 other cases the results were poor In 1 of these cases the ureter opened into the diverticulum and in another case four diverticula were excised leaving a small contracted bladder

30 DAY R V and Martin H W Vesical Diverticulum I A M A 112 509-513 (Feb 11) 1939

Bilharziasis—Campbell³¹ stated that vesical bilharziasis is not common in the United States but is found chiefly in the Mediterranean countries and is endemic in Egypt, Greece, Syria, Uganda, Turkey and South Africa. The antihelminthic hospitals of Egypt alone treat the condition in over a quarter of a million cases a year. In the United States about 30 cases have been reported.

Three trematodes of the genus *Schistosomum* which infest the human body are first *Schistosomum mansoni*, second, *Schistosomum japonicum* and last *Schistosomum haematobium*, which is of chief interest to the urologist because the outstanding lesions caused by its presence are in the urinary tract. These parasites are found especially in Africa, India, Mesopotamia, Madagascar, Greece and Japan. Their ova, unlike those of both the previously mentioned species, have terminal spines and may be found both in the urine and in pathologic tissues.

Although the urinary tract, especially the bladder, is the most common site of the lesions, *Schistosomum haematobium* may also affect the epididymis, prostate gland, seminal vesicles, corpora cavernosa, corpus spongiosum, urethra and female genitalia.

The parts of the bladder most commonly involved by bilharzial lesions are the trigon, the ureteral orifices and the posterior wall. The summit of the bladder is usually the last site to be involved but in cases of advanced involvement may be the place where characteristic lesions are seen.

There may be few symptoms of the disease, after penetration of the cercariae, headache, malaise, fever and cough may occur, together with pruritus and erythema at the point of entrance. The urinary symptoms may occur from three or four weeks to several years after inoculation. Hematuria, the most constant symptom, is often the only one. It is usually terminal, and it may not occur if only deep-seated lesions are present. If secondary infection is present, irritability of the vesical neck will be present, and often there are suprapubic pain, chills and fever. A rather marked anemia with a low color index is often associated with the picture. There may be slight leukocytosis and eosinophilia.

Diagnosis in sections of the world where the disease is common is not difficult, but in parts where the condition is unusual the diagnosis may be dependent on competent pathologic examination of specimens at biopsy, in which ova are usually seen embedded in the tissues. Other methods of diagnosis are examination of the urine for ova, cystoscopic examination and roentgen examination. The ova are ovoid, about 140 microns in length and narrowed at one end, to which is attached a terminal spine. Cystoscopic examination reveals the rather typical lesions.

³¹ Campbell, D. A. Vesical Bilharziasis. A Case Report, *J. Urol.* 40: 59, 605 (Nov.) 1938.

previously described. Roentgen examination may show a dense homogeneous cloudlike shadow limited to vesical contour or to one or another part of the ureter and to the general thickening of the walls of the affected part on account of the presence of calcified eggs irregularly deposited but not in sufficient numbers or concentration to throw a dense calcareous shadow of the organ. Definite calcified demarcations are pathognomonic but cloudy shadows are only highly suggestive as chronic cystitis from other causes may produce them.

Emetine hydrochloride, papaverine, emetine periodide, antimony sodium thioglycolate, antimony thioglycollamide and carbon tetrachloride have all been used successfully. Christopherson found that the use of antimony and potassium tartrate killed the parasite and destroyed the viability of the ova. At that time he recommended the use of doses of $2\frac{1}{4}$ grams (0.14 Gm.) each until 20 to 30 grains (1.3 to 2 Gm.) had been used. Later a new compound called tuadin was found to cure bilharzia disease in the majority of cases. Campbell stated that Khalil and Betache recommended intramuscular or intravenous administration of 1.5 cc. on the first day, 3.5 cc. on the second, 5 cc. on the third and 5 cc. every other day until a total of ten injections or approximately 40 cc. had been given. Basing their conclusions on 1474 cases these investigators found the reactions to be practically negligible and only 4 per cent of the patients were not cured after completion of the course of treatment. In this group of 4 per cent an additional course of three injections was found to be sufficient.

Campbell reported a case of this condition in a 21 year old patient who was treated with tuadin.

(To Be Concluded)

News and Comment

Biological Photographic Association—The ninth annual convention of the Biological Photographic Association will be held September 14 to 16 at the Mellon Institute for Industrial Research, Pittsburgh. The program will be of interest to scientific photographers, scientists who use photography as an aid in their work, teachers in the biologic fields, technical experts and serious amateurs. It will include discussions of motion picture and still photography, photomicrography, color and monochrome films and processing, all in the field of scientific illustrating. Up-to-date equipment will be shown in the technical exhibit and the print salon will display the work of many of the leading biologic photographers in the United States and abroad.

The *Biological Photographic Association Journal* is published quarterly and constitutes a volume of about 250 pages, which is furnished free to members. Membership privileges include an authoritative question and answer service and the right to borrow loan albums and exhibits of scientific prints for study and display.

Further information about the association and the convention may be obtained by writing the secretary of the Biological Photographic Association, University Office, Elizabeth Steel Magee Hospital, Pittsburgh.

DIAGNOSIS OF RUPTURED ABDOMINAL AORTIC ANEURYSM

REPORT OF A CASE

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AND

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PHILADELPHIA

Rupture of an aneurysm of the abdominal aorta is of infrequent occurrence. The correct diagnosis of this accident has rarely been made. This study is based on a survey of the literature and a personally encountered case. Kampmeier¹ in 1936 reported 73 cases and reviewed the literature on the subject. He found 313 cases reported up to the time of his publication. Since his review, there have been reported 41 additional cases. The total number of cases in the literature is 427. We wish to add 2 cases, 1 of which is reported in detail. The autopsy records of the Mount Sinai Hospital since 1930 have revealed 1 case of rupture of an aneurysm of the abdominal aorta. The second case in the hospital records, described in this paper, makes a total number of 429 reported cases.

Cases of abdominal aneurysm fall into two major groups: those in which the aneurysm is observed before rupture and those in which there are symptoms attributable to rupture of the sac. The violent abdominal symptoms caused by a ruptured aneurysm make it necessary to consider this lesion as one of the possible causes of an acute abdominal catastrophe. The symptoms of rupture are often bizarre and the diagnosis difficult. It is our belief, however, that careful consideration of the clinical findings and proper selection of laboratory and roentgen studies may often lead to the correct diagnosis.

REPORT OF CASE

H. E. C., an obese white man aged 62, was first seen at 7:30 p. m. on June 3, 1938, complaining of excruciating pain of sudden onset in the left side of the abdomen and the left groin. At the onset of the pain he had gone into profound syncope and had a profuse involuntary bowel movement.

From the Mount Sinai Hospital.

1. Kampmeier, R. H.: Aneurysm of Abdominal Aorta. Study of Seventy-Three Cases. *Am. J. M. Sc.* **192**: 97-109, 1936.

The past history revealed the following items of interest (1) There had been vague digestive complaints for the past two years, usually relieved by sodium bicarbonate, (2) nephropexy on the right side had been performed two years previously, (3) an inguinal hernia on the left side had been repaired twice, (4) a few months previously the patient had been treated for prostatic enlargement, had had an indwelling catheter for ten days and subsequently had had cystitis, and (5) hypertension had been present for a number of years, the systolic blood pressure averaging 160 mm of mercury.

On the morning of June 3 the patient complained of a dull pain in the left groin, which persisted up to the onset of the sudden, agonizing pain.

When the patient was first seen, he was in extreme shock, pulseless, cold and clammy. The respirations were rapid and shallow, and the blood pressure was unobtainable. The abdomen was soft and not distended. He complained of severe pain when the left lower abdominal quadrant was palpated. A vaguely defined fixed, nonpulsatile mass could be felt in this region. There was no tenderness over the inguinal scar. No tenderness or rigidity was noted in either costovertebral angle. Peristalsis could be heard over the abdomen. No bruit was present.

The patient was taken to the hospital immediately. He vomited several times en route. On arrival, treatment for the shock was at once instituted, external heat, the Trendelenburg position, stimulants, morphine and intravenous dextrose saline solution being used. The tentative diagnoses considered were rupture of a peptic ulcer, ureteral stone and mesenteric vascular occlusion. An acute vascular crisis, especially mesenteric vascular occlusion, was considered the most probable diagnosis. A blood count at this time showed hemoglobin, 86 per cent, red cell count, 4,240,000 per cubic millimeter, white cell count, 24,400 per cubic millimeter, and polymorphonuclear cells, 78 per cent.

Within two hours the patient had responded to treatment. The skin was dry, the pulse was stronger and the blood pressure was 64 systolic and 38 diastolic. A flat plate of the abdomen was taken, and a fluoroscopic examination of the diaphragmatic areas was carried out with the patient in the semiupright position. The report of the roentgenologist follows: "There is no evidence of any gaseous distention of the large or the small bowel. Neither kidney can be distinctly visualized. There is evidence of a faint reniform shadow on the right side, but on the left side there is a suggestion of a mass in the renal region. The right psoas muscle can be faintly outlined. The left cannot be delineated. There is no roentgen evidence of stone in the kidney. Fluoroscopic examination reveals the diaphragm to be normally mobile. There is no evidence of gas under the diaphragm."

On his return from the x-ray room the patient was given an enema, which returned a few small fecal particles but no flatus.

The obliteration of the line representing the left psoas muscle was assumed to be due to a large congested and infarcted area of bowel. The extremely high white cell count was also in favor of the diagnosis of mesenteric vascular occlusion. In view of the patient's extremely critical condition, conservative treatment was given.

The following morning (June 4), his condition remained essentially unchanged. The pulse was still weak and rapid, the temperature was subnormal, and the blood pressure was 50 systolic (diastolic pressure?). An electrocardiogram taken at this time was reported as falling within normal limits. The urea content of the blood was 100 mg, the urea nitrogen content 25.5 mg and the chlorides 595 mg per hundred cubic centimeters. The Wassermann and Kahn reactions were negative. The patient was placed in an oxygen tent and treatment with morphine and parenterally administered fluids was continued.

p m he voided urine for the first time since admission. One ounce (30 cc) of cloudy urine was passed, containing a cloud of albumin many white blood cells and an occasional red blood cell but no sugar or acetone. The possibility of acute pancreatitis was thought of, and the urine was examined for diastase. This substance was observed in dilutions up to 1:50. It was thought that the marked oliguria was probably due to the continued low blood pressure which resulted in insufficient renal filtration pressure. During this day the patient began to show occasional periods of irrationality. The abdominal findings continued unchanged although some distention was beginning to appear. The mass in the left lower quadrant persisted. An enema given in the afternoon returned no feces or flatus. A blood count taken during the day showed hemoglobin 76 per cent, red cell count, 3,810,000 per cubic millimeter, white cell count, 27,500 per cubic millimeter and polymorphonuclear cells 80 per cent (30 per cent young forms).

At 9:30 a m on the following day (June 5) the patient was catheterized and the bladder was found empty. The value for urea nitrogen was 37.4 mg. The abdomen showed increased distention but peristalsis was still audible. A barium sulfate enema showed no abnormalities in the colon. An Abbott tube was introduced nasally, and a large amount of foul-smelling greenish black fluid was evacuated.

In view of the progressively downhill course and the increasing clinical signs of intestinal obstruction exploratory laparotomy was decided on. Our tentative preoperative diagnosis was mesenteric vascular occlusion.

Operation—With the region under local anesthesia a left lower rectus incision was made and the abdomen was explored. The descending colon and the sigmoid were not distended but were pushed forward by an enormous hematoma occupying the retroperitoneal area. Just above the bifurcation of the abdominal aorta a firm, pulsatile mass the size of an orange could be felt. The diagnosis of aneurysm of the abdominal aorta with rupture and retroperitoneal hemorrhage was obvious, and the abdomen was closed without further exploration.

The patient stood the operation well. On his return from the operating room his pulse was 104 and his blood pressure was 95 systolic and 60 diastolic. Later in the evening he was given a slow transfusion of 400 cc of citrated blood. At 10:45 p m his blood pressure was 110 systolic and 85 diastolic. He was catheterized at this time, and 1 ounce (30 cc) of urine was obtained. At 3 a m on June 6 he complained of sudden sharp abdominal pain, the pulse became rapid and feeble, and the blood pressure dropped. It was apparent that further hemorrhage was taking place from the ruptured aneurysm, and therapy was confined to complete morphinization. At 3:25 p m the patient died.

Autopsy (Abdomen)—When the abdomen was opened the most striking feature was the bulging anteriorly of the retroperitoneal tissues. The bulging extended upward to within a few centimeters of the diaphragm and laterally to about the midaxillary line. It was more prominent on the left side than on the right. The peritoneum over the bulging area was bluish and tense. On incision the bulging was seen to be due to an extreme infiltration of freshly clotted blood into the retroperitoneal tissues. The hemorrhagic process extended into and involved part of the mesentery of the small intestine. A great deal of clotted blood was observed around the lower pole of the left kidney and the left ureter. There was no free blood in the peritoneal cavity. The hemorrhage was seen to be due to the recent rupture of an aneurysm of the lower portion of the abdominal aorta. The

aneurysm was located about 15 cm above the bifurcation of the aorta. It involved primarily the posterior wall of the aorta and projected posteriorly to the left side. It measured 6 cm in diameter and was filled with fresh blood clot, which was easily separable from its wall. About 2 cm below the upper boundary of the aneurysm a partially detached atheromatous plaque was seen. This area communicated directly through the wall of the aneurysm to the densely infiltrated retroperitoneal tissues. The wall of the sac was of about the same thickness as the uninvolved aortic wall, averaging about 3 mm. Both the sac and the aortic



Fig. 1—Retroperitoneal tissues removed en masse showing retroperitoneal hemorrhagic infiltration

wall showed a moderate amount of atheromatous change, but no ulcerations were present except at the point of rupture.

Microscopic Observations—The pancreas showed fatty infiltration. The kidneys showed arteriolosclerosis, arteriosclerosis and cloudy swelling. There were marked congestion and cloudy swelling of the liver. The spleen showed marked congestion and focal hemorrhage. There was cloudy swelling of the adrenal glands. Medial scarring of the aorta was observed.

DIAGNOSIS

Most ruptured abdominal aortic aneurysms, as in our case, are diagnosed either at the operating table or at autopsy. This lesion has been mistaken for many diseases causing acute abdominal symptoms. Study of the case reports in the literature shows that ruptured abdominal



Fig 2—Aorta opened showing the aneurysmal sac.

aortic aneurysm has been variously diagnosed as ruptured peptic ulcer, ureteral calculus, volvulus of the pelvic colon, acute pancreatitis, mesenteric vascular occlusion, acute intestinal obstruction, perinephritic abscess, and psoas abscess.

Ruptured Peptic Ulcer—A history of gastric complaints is often found in cases of abdominal aneurysm, particularly if the aneurysm is

in the region of the celiac axis Osler² mentioned the fact that gastric symptoms may be early and deceptive Pressure on nerve plexuses may cause a boring type of pain and spasm similar to those caused by a penetrating ulcer The initial collapse of ruptured ulcer may simulate the shock of ruptured aneurysm Rarely, as in the case reported by McLean and Fiddes,³ the rupture may be intraperitoneal, with all the signs of sudden acute peritonitis Often it is difficult or impossible to palpate the aneurysm because of variations in its location and size and

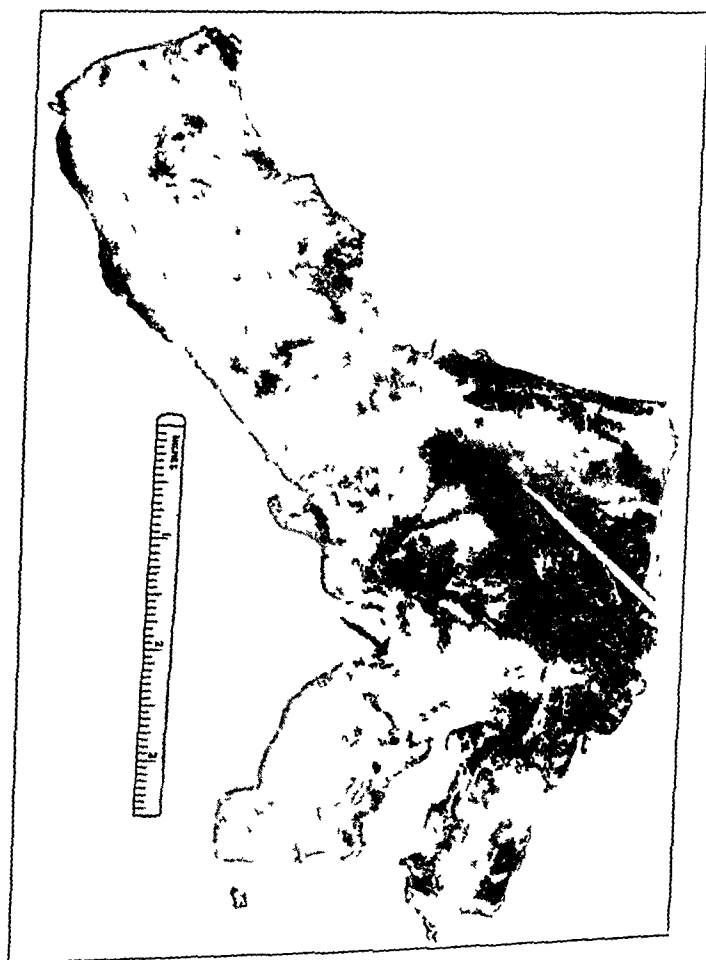


Fig 3—Aorta opened Note the probe in an opening in the aneurysm

because of the fact that expansile pulsation may be either present or absent Such pulsation is usually not present, since the wall of the sac is frequently partially obliterated by a thick, laminated clot

² Osler, W The Principles and Practice of Medicine, ed 12, rev 11 L T McCrae, New York, D Appleton-Century Company, 1935

³ McLean, J A, and Fiddes, J Two Cases of Sudden Death from Rupture of Aorta and from Rupture of an Abdominal Aneurysm, M J Australia 1: 87-809, 1929

Ureteral Calculus—The radiation of pain in cases of ruptured aneurysm may be similar to that of ureteral colic. Since the rupture is nearly always retroperitoneal, irritation of the spinal nerves and sympathetic plexuses by the retroperitoneal hemorrhagic infiltration may produce pain of variable distribution. In a case reported by Willis⁴ the typical symptoms of ureteral calculus were present. At operation a retrorenal hematoma was found, and autopsy disclosed a ruptured saccular aneurysm of the abdominal aorta. The clinical picture of severe shock and hemorrhage should, however, eliminate the diagnosis of ureteral colic in most cases.

Volvulus of the Pelvic Colon—Intermittent bleeding from a small rupture may simulate the colicky pain of volvulus. In addition, the retroperitoneal hemorrhage may produce an abdominal mass. Cuny⁵ reported a case in which, because of colicky pain, an abdominal mass and bloody diarrhea, a diagnosis of volvulus was made. At operation a ruptured aneurysm and a retroperitoneal hematoma were found. Cuny stated that preoperatively an area of ecchymosis was seen in the flank. He expressed the opinion that not enough significance was attached to this observation and emphasized that the sign may have diagnostic importance.

Acute Pancreatitis—Retroperitoneal hemorrhage from a ruptured aneurysm may produce all the symptoms of acute pancreatitis, especially if the aneurysm or sanguineous infiltration is in the region of the pancreas. In our case, presumably because of irritation of the pancreas by the extravasated blood the diastase content of the urine was increased. This is the first time this observation has been recorded. Bazy and Calvet⁶ reported a case in which laparotomy was performed after a diagnosis of ruptured ulcer had been made. A hemorrhagic infiltration of the pancreas was discovered and, in addition, an ovoid nonpulsatile mass dorsal to the pancreas was present. The latter was thought to be a pancreatic cyst. Autopsy revealed a saccular aneurysm of the aorta with rupture directly into the substance of the pancreas.

Mesenteric Vascular Occlusion—The sudden onset of acute abdominal pain, collapse and vomiting and the presence of a high leukocyte count may lead to the diagnosis of mesenteric vascular occlusion. This

4 Willis P. W. Ruptured Aneurysm of Abdominal Aorta with Left Retrorenal Hematoma. Symptoms Suggestive of a Right Ureteral Calculus. *S. Clin. North America* **10** 1231 1234 1930.

5 Cuny J. Rupture d'un anévrysme de l'aorte abdominale simulant un volvulus du colon pelvien. *Lyon chir.* **34** 58 59 1937.

6 Bazy L. and Calvet J. Syndrome abdominal aigu par anévrysme pancréatique (pancréatite aiguë hémorragique) coïncidant avec un anévrysme de l'aorte abdominale. *Mém. Acad. de chir.* **61** 1336-1340 1935.

disease occurs in patients of the same age group as most of those with ruptured aneurysm, and patients with either condition usually show evidence of arteriosclerosis and hypertension. Arteriosclerosis is considered by many observers to be the major etiologic factor in abdominal aneurysm, as contrasted with thoracic aneurysm, of which syphilis is the usual cause.⁷ The intrasaccular thrombus in aneurysm may obstruct the orifice of the superior or the inferior mesenteric artery and produce the complete syndrome of mesenteric vascular occlusion. In a case reported by Gilmour and McDonald⁸ this picture was produced by occlusion of the superior mesenteric artery in the sac of an abdominal aortic aneurysm.

Acute Intestinal Obstruction—Paralysis of the bowel in cases of ruptured aneurysm may occur as a result of the retroperitoneal hemorrhage, particularly if the leakage is slow and the patient survives for a few days. Vomiting and constipation may be present, as they were in our case. In a case reported by Jaffé⁹ a diagnosis of acute intestinal obstruction was made because of vomiting, constipation and signs of peritoneal irritation. Autopsy revealed the usual retroperitoneal hematoma of ruptured aneurysm.

Perinephritic Abscess—Accumulation of blood in the loin from a ruptured aneurysm may present the picture of a perinephritic abscess. Rusche and Bacon¹⁰ reported a case in which there were pain in the loin, a tender mass in this area, obliteration of the line representing the psoas muscle on roentgen examination, nausea and distention. A lumbar incision disclosed a huge hematoma, and autopsy revealed a ruptured saccular aortic aneurysm. A report by Peel¹¹ presented a similar case, in which, in addition to the other symptoms mentioned, the typical syndrome of uremia was present.

Psoas Abscess—A retroperitoneal hemorrhage may burrow along the psoas muscle and present in Scarpa's triangle, simulating a psoas

7 Neely, J. M. Ruptured Abdominal Aorta. Clinico-Pathological Study of Five Cases from Lancaster County Medical Museum, Nebraska. *M. J.* **22**: 370-377, 1937. Bell, E. T. A Text-Book of Pathology, ed. 3, Philadelphia, Lea & Febiger, 1938.

8 Gilmour, J., and McDonald, S., Jr. Aneurysm of Abdominal Aorta and Thrombosis of Superior Mesenteric Artery Associated with Bullet Wound of Lung. *Brit. M. J.* **2**: 587-589, 1932.

9 Jaffé, H. Rupture of Abdominal Aneurysm Simulating Acute Intestinal Obstruction. *Brit. M. J.* **1**: 1173, 1925.

10 Rusche, C. F., and Bacon, S. K. Ruptured Abdominal Aortic Aneurysm Simulating Perinephritic Abscess, with Report of a Case. *Brit. J. Urol.* **7**: 330-332, 1935.

11 Peel, J. H. Rupture of Aneurysm of Abdominal Aorta. *Lancet* **1**: 512-1937.

abscess Eckert and Baker¹² reported a case in which the diagnosis of psoas abscess was made because of abdominal, lumbar and femoral pain, nausea, vomiting and a pulsatile mass in the femoral region. Lumbar incision revealed a massive hematoma from a ruptured aneurysm of the abdominal aorta.

COMMENT

Although we are concerned in this report with a study of ruptured abdominal aneurysm it is interesting in order to illustrate the difficulty of the diagnosis, to note a few of the conditions with which unruptured aneurysm of the abdominal aorta has been confused. This condition has been variously diagnosed as tumor of the small bowel,¹³ tumor of the spinal cord,¹⁴ spinal arthritis, tumor of the liver, carcinoma of the stomach, pancreatic cyst, malignant tumor of the retroperitoneal nodes, renal tumor¹ and, in fact, almost every intra-abdominal and retroperitoneal syndrome known.

A clinical analysis of the cases reported in the literature and of our personal case has led us to the opinion that certain features of this condition are sufficiently distinctive to bring the condition to mind as a possibility in the diagnosis of obscure acute abdominal syndromes. Two general features are important: (a) the fact that ruptured aortic aneurysm is an acute vascular disease and presents features that characterize vascular crises in general and (b) the fact that the retroperitoneal hemorrhage usually present causes certain signs and symptoms that differentiate it from intraperitoneal disease.

The pain of all vascular crises is sudden and violent. The great majority of ruptured aneurysms evidence themselves first with sudden, agonizing pain, usually abdominal but occasionally lumbar as well. Accompanying the pain is shock, usually severe and persistent. The clinical signs of intraperitoneal disease are slight or absent, the lack of tenderness or rigidity being in great contrast to the severity of the abdominal symptoms. A localized, fixed mass is often present. If this shows expansile pulsation and a bruit, the diagnosis is obvious. Unfortunately in many cases neither of these signs is present. Nausea, vomiting and distention due to irritation of the retroperitoneal nerve plexuses are common but not marked. Intestinal peristalsis may be but little affected.

12 Eckert G. A. and Baker R. E. Rupture of Aneurysm of Abdominal Aorta from Surgical Viewpoint. Report of Two Cases. *U. S. Nav. M. Bull.* **29** 667-671 1931.

13 Petridis P. Sur cinq cas d'anévrysme rompu de l'aorte dont quatre de l'aorte abdominale et un de l'aorte thoracique. *J. Egyptian M. A.* **13** 44-64 1930.

14 Weingrow S. M. and Bray W. A. Aneurysm of Abdominal Aorta. Case Report. *Am. J. Roentgenol.* **36** 104 196 1936.

The leukocyte count is usually high, a common finding in cases of internal hemorrhage. This observation has been noted by many observers and was a feature of our case.

The roentgen studies are most significant. Perforation of a hollow viscus can be ruled out in the majority of cases by the absence of free gas under the diaphragm. A flat plate of the abdomen often shows obliteration of the line representing the psoas muscle.¹⁵ This observation directs attention toward the retroperitoneal area. Volvulus and obstruction of the large bowel can be immediately dismissed if the colon is roentgenographically normal after a barium sulfate enema. The most important roentgen study in cases of suspected aneurysm is that which gives a lateral view of the lower thoracic and the lumbar vertebrae. Erosion of the vertebral bodies with preservation of the intervertebral disks¹⁶ in the presence of suggestive symptoms is almost pathognomonic of aneurysm.

The finding of a moderately increased diastase content of the urine, as far as we have been able to determine, has not been previously recorded. Since the pancreas is entirely retroperitoneal and the hemorrhage present in ruptured aneurysm is similarly retroperitoneal, pancreatic irritation, as evidenced by increased diastase in the urine, should be helpful in the diagnosis of this lesion.

Treatment—The treatment of abdominal aneurysm has given most disappointing results. For many years attempts have been made to attack this lesion by ligation, both proximal and distal, by proximal compression with aluminum and fascial bands, by the Moore-Corradi method of wiring and electrolysis and by the introduction of Colt's cages. Reid¹⁷ reported 4 cases of abdominal aortic aneurysm in which ligation with tapes and metallic bands was done. All the patients died, 3 from secondary hemorrhage caused by cutting through of the aorta by the band. The same author reported 8 cases of abdominal aneurysm wired by the Moore-Corradi method, with no cures. Colt¹⁸ introduced a wire cage into the aneurysm through a specially designed stilet in 2 cases, both the patients died. Power¹⁹ had more success with this

15 Held, I. W., and Goldbloom, A. A. Three Rare Intra-Abdominal Cases. *S. Clin. North America* **14**: 389-405, 1934. Rusche and Bacon.¹⁰

16 Brailsford, J. F. Aneurysm of Abdominal Aorta. Diagnosis by Lateral Radiograph of Spine, *Brit. J. Surg.* **14**: 369-371, 1926. Weingrow and Bray.¹⁴

17 Reid, M. R. Aneurysms in the Johns Hopkins Hospital. All Cases Treated in the Surgical Service from the Opening of the Hospital to January 1922. *Arch. Surg.* **12**: 1-74 (Jan., pt. 1) 1926.

18 Colt, G. H. Aneurysm of Abdominal Aorta, *Brit. J. Surg.* **13**: 169-171, 1925.

19 Power, D. A. The Palliative Treatment of Aneurysm by "Wiring" with Colt's Apparatus, *Brit. J. Surg.* **9**: 27-36, 1921.

method, having 4 survivals in 11 cases. Brooks²⁰ treated an aneurysm successfully by proximal ligation, using a broad fascial strip. Two other successful ligations have been recorded,²⁰ 1 by Matas and 1 by Vaughan.

This brief review of the results of surgical treatment of unruptured aneurysm of the abdominal aorta indicates that once this lesion has ruptured the condition becomes practically hopeless. In only 1 case reviewed by us has direct attack been made on a ruptured aneurysm. This was a case reported by Petridis,¹³ death of the patient followed immediately. It is within the realm of possibility that absolute rest may suffice to seal the perforation in the aneurysmal sac and may result in recovery. A case reported by Leriche¹ in which a ruptured aneurysm was found to have sealed itself off by the formation of a second, false aneurysm which did not rupture until operative intervention was attempted illustrates the rationale of judicious neglect. Certainly the results of nonoperative treatment can be no worse than those of operation.

CONCLUSIONS

1 Ruptured abdominal aortic aneurysm should be considered in the diagnosis of any puzzling acute abdominal crisis.

2 The distinctive features are those of vascular crisis, shock and retroperitoneal hemorrhage.

3 Obliteration of the line representing the psoas muscle and erosion of the vertebral bodies with preservation of the intervertebral disks are important roentgen observations.

4 A high leukocyte count is constant.

5 The diastase content of the urine may be moderately elevated.

6 The treatment advised is nonoperative.

20 Brooks B. Ligation of the Aorta. A Clinical and Experimental Study. *J A M A* **87** 722-725 (Sept 4) 1926.

21 Leriche R. Operations pour rupture d'anévrysme de l'aorte avec formation d'hématome enkysté à évolution lente (deux observations), *Bull et mem Soc nat de chir* **60** 876-878 1934.

TRAUMATIC FAT EMBOLISM

REPORT OF TWO CASES WITH RECOVERY

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NEW YORK

Fat embolism is a definite, well established disease entity which is neither new nor infrequent¹ Over seventy-five years ago the condition was reported in man, its clinical aspects were noted, its physiologic alterations described and the postmortem observations recorded Many articles have appeared in the literature since that time covering the various aspects of the condition From them one is able to draw a fairly definite and accurate picture of what happens in a person in whom this complication develops The term complication is used because in nearly all cases it is a complication of some other condition in the body, the exception to this being fat embolism due to intramuscular injections of medicated oils that inadvertently enter the blood stream The conditions to which it is a complication are diversified and include osteomyelitis, nephritis, burns, orthopedic operations, operations on and injuries to fatty tissues, fractures, contusions and degenerative processes in the body Interest here is in traumatic fat embolism, especially that due to a fracture

That the introduction of liquid fat into the blood stream follows injuries to the skeletal system with surprising frequency has been definitely proved at autopsy Not all fat embolisms, however, are of such severity as to cause death or even to produce clinical symptoms Many persons who live have few or no symptoms, and many others who have symptoms recover without the exact nature of the condition being diagnosed

Read before the Harlem Surgical Society, Oct 19, 1938

From the Surgical Service of the Harlem Hospital, Dr Louis F Wright
Director

1 (a) Gauss, H The Pathology of Fat Embolism, Arch Surg 9 593 (Nov pt 1) 1924 (b) Studies in Cerebral Fat Embolism with Reference to the Pathology of Delirium and Coma, Arch Int Med 18 76 (July) 1916 (c) Groskloss, H H Fat Embolism, Yale J Biol & Med 8 59, 175 and 279 1935 (d) McCaster J C Fat Embolism A Case Report of Cerebral Involvement, Wisconsin M J 36 724, 1937 (e) Warthin, A S Traumatic Lipaemia and Fatty Embolism, Internat Clin 4 171 1913 (f) Watson A J Fat Embolism Report of a Case with Review of the Literature Brit J Surg 24 676, 1936 (g) Wright, R B Fat Embolism, Ann Surg 96 75 1933 (h) Vance, B M Significance of Fat Embolism Arch Surg 23 426 (Sept) 1931

There has been dispute as to the origin of the fat, it being claimed by some that there is not enough fat in any long bone of the body to cause death even if all of it should enter the circulation. Whether the injured bone is the sole source of the fat or whether there is some additional alteration in the normal lipid content of the blood, the chief source of the fat is the injured bone. In that area the fat globules are liberated and are either drawn or forced by compression into the torn haversian veins. A small amount may reach the circulation by way of the lymphatics. The fat passes to the right side of the heart and from there enters the pulmonary circulation, where it becomes lodged in the finer arterioles and capillaries. If the amount of fat is too great it may act much the same as an air embolus on the heart and cause death before it reaches the lung.

As the pressure in the pulmonary circulation rises, many of these fat globules are forced on through the capillaries of the lungs and are carried to the left side of the heart from whence they may go to any part of the body but chiefly to the brain and kidneys.

To understand the symptoms produced by fat embolism, it is necessary first to understand the pathologic process. The entire clinical picture is the sum total of the effects of numerous small, transient emboli lodged in capillaries, each of which has practically the same unit pattern, the symptoms produced being dependent on the number, location and duration of the emboli. This unit pattern consists essentially of a small vessel obstructed by a fat globule and surrounded by extravasated blood causing focal anemia, edema or necrosis. Later various white blood cells and phagocytes appear in the area to help in repair.

Shortly after the fat enters the systemic circulation it begins to be excreted by the kidneys and can be detected in the urine. This process of elimination is aided by the absorptive and phagocytic actions of various liver cells and by phagocytes and giant cells which invade the damaged areas. Enzymes in the blood stream aid the process by saponification of the fat.

Although fat globules reach practically all parts of the body, symptoms are usually referable to the lungs and brain. Consequently, there are two types of fat embolism clinically, the pulmonary and the cerebral depending on the preponderance of one group of symptoms over the other. However, no sharp line can be drawn between the two as there are some pulmonary and some cerebral symptoms in each case.

Symptoms develop within a few hours to a few days. There is always a free interval, a kind of incubation period which is an aid in making a differential diagnosis. With the pulmonary type of embolism respiratory and cardiac embarrassment are evident. There are dyspnea, cough, cyanosis, restlessness and a feeling of constriction in the chest. Air hunger may develop. The pulse is rapid and may be irregular. The temperature may be normal but in the great majority of cases it is

elevated. The sputum becomes frothy and may be blood streaked. Stained with scarlet red or sudan III, it may show fat globules. Rales are heard scattered over the pulmonary fields as a result of mild or severe pulmonary edema. The right side of the heart is put under considerable strain and is usually dilated. Blood pressure is most frequently low.

With the cerebral type, drowsiness, disorientation, stupor and coma appear, in addition to some respiratory symptoms. Hallucinations or delirium may be evident. There are no persistent localizing neurologic symptoms, but transient muscle spasm, tremors, convulsions and paralyses may occur. All are indicative of widespread cerebral involvement and irritation. Incontinence of feces and urine often develops. In most cases of the cerebral type and in some of the pulmonary type of embolism petechial hemorrhages of the skin and conjunctivas develop. This is a sign of great diagnostic importance.

As previously stated, nearly all persons with fat embolism recover without a diagnosis being made, or a diagnosis is made after the post-mortem examination. Consequently it is not possible even to approximate the true mortality rate. On the basis of the cases reported in the literature, this has been placed at from 85 to 90 per cent. There are relatively few cases in which recovery was reported, only 1 such case could be found in the American literature. Two patients with this condition were seen in the wards of the Harlem Hospital during the past two years, both of whom recovered. These 2 cases are here reported.

REPORT OF CASES

CASE 1—T. B., a 22 year old Negro student, sustained a fracture of both bones on the right leg in an intercollegiate basketball game near midnight, Feb. 13, 1937. He was brought to the Harlem Hospital immediately with his leg in an improvised splint. His general condition was good. There were no signs of injury aside from swelling, tenderness and ecchymosis of the right leg. Roentgen examination confirmed the diagnosis of fracture of the tibia and fibula. The temperature was 98 F, the pulse rate 68, the respiratory rate 18 and the blood pressure was 132 systolic and 84 diastolic. The urine and the blood count were normal. A circular cast was applied from the middle of the thigh to the toes without anesthesia. The cast was split anteriorly in its entire length.

The next morning the patient's condition was the same, but by afternoon the temperature had risen to 102.4 F. The pulse rate was 88, and the respiratory rate 22. The white cell count was 17,600, with 84 per cent polymorphonuclear. The patient was somewhat drowsy.

On the evening of the following day, two days after admission, drowsiness was marked, and dyspnea and cyanosis were present. The temperature was 102 F, the pulse rate 92 and the respiratory rate 40. There were numerous rales and coarse crepitant rales heard throughout both pulmonary fields. A diagnosis of fat embolism was made.

The next morning the temperature was 101 F and the respiratory rate 32. Rales were present but were fewer. Drowsiness had increased but the patient was awakened. A physician from the pneumonia service who was called in

pneumonia was not present. Culture of the sputum in mouse peritoneum was negative for pneumococci. Oxygen was given by nasal catheter. A roentgenogram of the chest, made with the portable apparatus, showed a few patches of consolidation scattered over both pulmonary fields and a general haziness that is often seen in cases of pulmonary edema. Two petechiae were noted on the conjunctiva of the right lower lid. By evening they had become much more numerous. None was found on the skin. There was some expectoration of bloody sputum. Cultures of the blood were taken and later reported to be negative.

On the fourth day after injury the temperature was almost normal, the dyspnea had disappeared, and all signs in the chest were gone. The subconjunctival hemorrhages continued for several days longer. All examinations of the urine were negative for fat.

Considering the trauma, the free interval, the onset of drowsiness, the dyspnea and cyanosis, the rales indicative of pulmonary edema, the

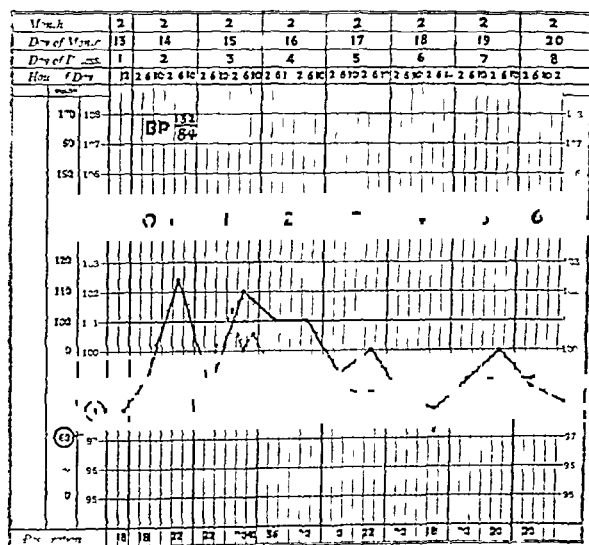


Fig 1 (case 1) —Temperature chart

petechial hemorrhages of the conjunctiva, the brevity of the condition, and the absence of any other disease that would produce these symptoms, the diagnosis of fat embolism of the pulmonary type was justified.

CASE 2—B A, a 19 year old Negro youth was admitted to the surgical service of the Harlem Hospital at 2:30 p.m. on June 27, 1938, one hour after being hit by an automobile. He had been transported a distance of about half a mile with his legs in Thomas splints. There was no history of bleeding or unconsciousness.

pressure 150 systolic and 100 diastolic. The white cell count was 6,700, with 68 per cent polymorphonuclears, 30 per cent lymphocytes and 2 per cent transitionals. The red cell count was 4,700,000, with a hemoglobin content of 70 per cent. The Kahn reaction of the blood was negative on two occasions. Roentgenograms of the legs showed a fracture of each tibia at the junction of the middle and the lower third, in good position.

The patient was taken to the operating room at 4 a. m., and a circular plaster of paris cast was applied to each leg from the middle of the thigh to the toes, with the knee slightly flexed and the ankle at right angles. The casts were split anteriorly in their entire length. No anesthesia was used. The patient was returned to the ward at 5:30 a. m. in good condition.

At 11 a. m., about ten hours after the injury, the patient seemed to be in a daze. He complained of pain in the back and abdomen. He had been unable to void urine since admission. At 5 p. m. he was extremely restless. The bladder was catheterized, and 6 ounces (177 cc.) of amber-colored fluid was obtained. The urine was normal. At 7 p. m. the patient calmed down and was sleeping. At 8:30 p. m. he seemed irrational and was talking at random and complained of pain in the back and both loins. The temperature was 102.8 F., the pulse rate 110, the respiratory rate 24 and the white cell count 16,400, with 88 per cent polymorphonuclears. Roentgenograms of the spine and pelvis were normal. Codeine and phenobarbital were given.

The patient slept fairly well, but the next morning, June 28, he was still disorientated, and by 9 a. m. he was in a deep stupor and could not be aroused. There were spasmodic contractions of the upper extremities and occasional slight tremors of the body. There was incontinence of urine. A spinal tap yielded clear fluid under a slight increase of pressure. The abdominal wall was rigid, retracted and markedly tender. The temperature at this time was 101.6 F., the pulse rate 102 and the respiratory rate 22. There were numerous petechial hemorrhages over the upper part of the chest. One such hemorrhage was seen on the conjunctiva of the left eye. There were no other neurologic symptoms. A diagnosis of fat embolism of the cerebral type was made. Examination of the urine gave negative results. The blood showed 174 mg. of cholesterol and 197 mg. of fatty acids per hundred cubic centimeters. A continuous infusion of 5 per cent dextrose in physiologic solution of sodium chloride was started, and alcohol sponges were ordered for the control of high temperatures. The patient remained in this comatose condition throughout the day and night. The temperature rose to 104.4 F. in the afternoon and fell gradually to 101.8 F. by the next morning. The respiratory rate was 36 in the afternoon, 40 in the evening and 30 the next morning. The patient continued to have urinary incontinence. Roentgenograms of the chest taken at this time were not satisfactory but were sufficiently clear to eliminate the presence of pneumonia. Physical signs of pneumonia were absent.

On the morning of June 29, two days after admission, the patient was still comatose. The temperature was 101.8 F., the pulse rate 106 and the respiratory rate 30. The petechial hemorrhages had become much more numerous on the upper part of the chest and had begun to appear on the neck and lower part of the face and abdomen. A biopsy was taken from the chest in an area of many numerous petechiae.

Later in the morning the patient was more reactive to painful stimuli. In the afternoon he seemed to come out of the coma and at times moved his head as if attempting to talk, but no sound was audible. By evening, however, he had again lapsed into coma, and there was fecal as well as urinary incontinence.

The following morning, June 30, the temperature had fallen to 101 F. In the evening to 102.4 F. Chemical examination of the blood showed 13.5 per cent

creatinine, 15 mg of urea nitrogen and 100 mg of sugar per hundred cubic centimeters of blood

On the morning of July 1 the patient's condition was precarious. The temperature was 104 F, the pulse rate 160 and the respiratory rate 36. The petechial hemorrhages had increased in number and were present on the arms and forearms. The pupils were in midsyllatation, equal and sluggish in response to light. There was a soft systolic murmur at the apex of the heart. Respirations were shallow, and breath sounds were suppressed throughout the chest. Cultures of the blood and of the spinal fluid were made, the spinal fluid was examined and a Felix-Weil test was done. The results of all were later reported to be negative. By evening the temperature was 105.4 F, the pulse rate 130 and the respiratory rate 30.

Throughout the next day, July 2, the temperature remained around 105 F and the respiratory rate from 32 to 40. Urinary and fecal incontinence continued.

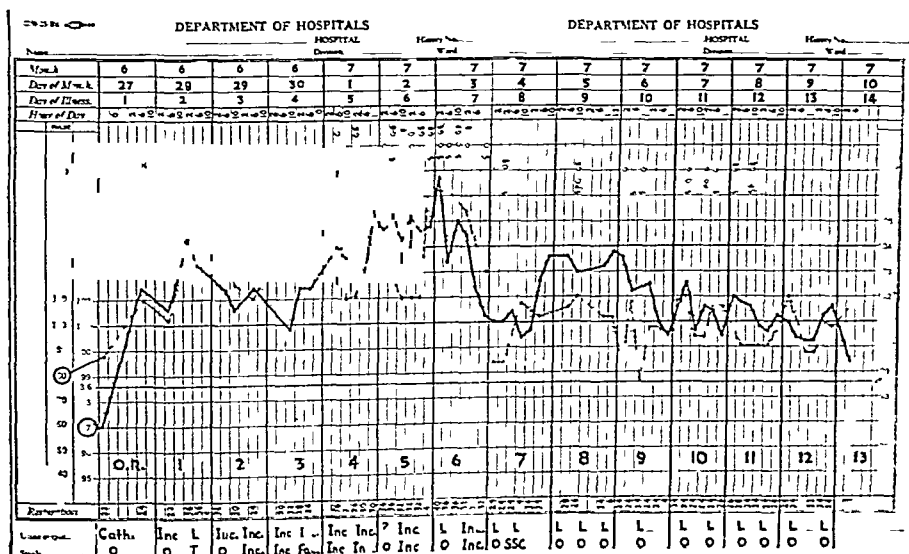


Fig 2 (case 2) —Temperature chart Inc stands for incontinence L for lost SSC for soapsuds elysis, Cath for catheterized O, for none

On the morning of July 3, at 2 a m the temperature was 106.8 F the pulse rate 154 and the respiratory rate 40. At 6 a m the temperature had fallen to 103.4 F, and at 6 p m to 101 F. Urinary and fecal incontinence were still present. In the evening the patient rallied came out of the coma and attempted to speak. He drank 50 cc of water the first he had taken by mouth since the day of admission.

On July 4 his condition was improved although the temperature rose in the evening to 103.6 F. On this day the patient regained control of the bladder and rectal sphincters after five days of incontinence. The rigidity in the arm was entirely absent, but there was extreme weakness in the muscles.

On July 5 he was still conscious and more alert and responded to questions with a nod of his head. He was able to drink water in small amounts. The temperature was 103.6 F, the pulse rate 100 and the respiratory rate 32.

On July 6 the temperature was 103.6 F. The patient was alert but throughout the morning failed to answer questions. For the first time the urine gave a positive reaction for nit

On July 7 there was considerable improvement. The temperature ranged between 102.6 and 104 F, and the respiratory rate was 24.

On July 8 the condition was improved, and the patient was more alert. The hemorrhagic areas remained only on the shoulders and neck, but instead of areas of discoloration there were present brown, flat-topped, firm papules about a millimeter in diameter.

Gradual improvement continued through the next two days, although the temperature remained at 101.4 F. On the morning of July 10 the temperature was 99.4 F, the pulse rate 106 and the respiratory rate 24. On July 11 the temperature was 99.2 F. The patient began to mumble answers to questions and took fluids by mouth frequently. Intravenous infusions were stopped.



Fig. 3 (case 2) —Petechial rash

During the next week the temperature ranged between 99 and 100 F, and the general condition gradually improved. The patient began to regain the use of his arm, and the hemorrhagic areas were faint. During the nights and occasionally in the days the patient showed periods of boisterousness and anger. Otherwise convalescence continued to be uneventful.

There can be no doubt but that this case is one of traumatic fat embolism of the cerebral type. The symptoms are exactly similar to those described in the cases in which the diagnosis was proved at autopsy. The extensive petechial hemorrhages and the fat in the urine make the diagnosis certain.

The treatment for fat embolism has been concisely expressed by Vance,¹¹ who stated: "As a rule, when the fat has entered the blood stream, the result must be left to the natural defenses of the body."

only symptomatic treatment can be applied." This was true in the present case. A continuous infusion of 5 per cent dextrose in physiologic solution of sodium chloride was given for two full weeks the amount averaging about 4 liters a day. Alcohol sponges at intervals of four hours were given to combat high temperatures. Excellent nursing care was administered day and night, and this aided more than any other therapeutic measure in the recovery.

It is interesting to speculate as to the part played by the casts in the duration and severity of the illness, and this patient had on two casts. The veins of the haversian canals do not collapse as veins elsewhere when torn across but remain open and render access to the circulation easy for the fat globules. The extravasation of blood and serum into the tissues exerts a pressure on this liberated fat, tending to force it into the veins. If a cast is applied before the tissues about the injured bone have reached their maximum swelling the continued extravasation into the tissues causes the pressure to be increased to a tremendous extent and can well be a factor in increasing and prolonging if not in actually causing the introduction of fat into the circulation. More can be done in preventing than in treating fat embolism and one of the most important points is the careful handling and manipulation of injured bone, as has been pointed out by all writers on the subject. To this can be added the avoidance of any constricting appliance that will increase the intraosseous pressure until after the maximum swelling has been reached. After the diagnosis had been made in this case, the casts should have been removed and the legs left in basket splints until the symptoms of embolism had cleared.

The papular change in the petechiae has not been described before. A biopsy of the skin was made, but nothing of significance was found. It seems possible, however, that these papules represented foreign body reactions to the fat emboli lodged in the vessels of the skin.

Another interesting development in this case was the onset of severe pain in the loins and abdomen twenty-four hours after admission. The abdominal pain and rigidity were so severe that had they been present on admission an exploratory laparotomy would most surely have been done. The pain in the loins was associated with the fact that on catheterization eighteen hours after injury only 6 ounces of urine was obtained showing a suppression. These symptoms pointed to severe involvement of the renal and mesenteric vessels.

COMMENT

It is hoped that these 2 cases will help to dispel the idea of the rarity and hopelessness of fat embolism and cause those entrusted with the treatment of the injured to bear the condition in mind. War has called it a neglected branch of surgery. There is no reason for its continuance as such.

ANEURYSM OF THE SPLENIC ARTERY

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Aneurysm of the splenic artery is a rare disease. It is so dangerous that only early diagnosis and proper treatment can prevent a tragic end. It is seldom diagnosed when encountered clinically, because it is not considered in the differential diagnosis. The entity, because of its rarity, is seldom discussed in the current literature and in many instances is not mentioned in textbooks. It is for these reasons that the following report is presented.

REPORT OF CASE

A white woman aged 30 was first seen about 9 p. m. on January 14, complaining of mild pain in the upper part of the abdomen. She had been well until one week prior to examination (approximately January 7), when she noticed roughness of the throat and "sore glands in the neck." This condition subsided within a few days. She continued to be fairly well until January 13, when she "just didn't feel right." She had the same peculiar feeling on the morning of January 14, and during the latter part of the afternoon she noticed mild aching pain in the upper part of the abdomen. The pain did not radiate. Urgency and frequency of urination were observed. The patient had her supper and about two hours later vomited. There was no fresh blood or coffee ground material in the vomitus. The abdomen became slightly distended and with an enema considerable flatus and dark brown formed stool were passed, with some relief. The abdominal pain and the urgency and frequency of urination persisted.

The systemic review gave negative results except for the following observations. There was moderate dyspnea on exertion. The stools had been dark since the patient had begun taking medicine for "anemia." Since the onset of the present illness urgency and frequency of urination had been present, but there was no burning. Only a few drops to a small amount of urine was passed each time. There was no difficulty in starting the stream. The menstrual period occurred regularly every twenty-eight days. The last period had started December 20.

The patient had had rheumatic fever when a child and since then had had a "bad heart" and had always been sickly. An appendectomy had been performed when she was 12 years of age, and a cesarean section and ligation of tubes had been done when she was 28, because of the cardiac condition. She had had pyelitis six months prior to examination.

The temperature was 98.4 F., and the pulse rate was 70. The patient was well nourished and fairly well developed. She was in bed but was neither acutely

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ill nor in distress. The skin, conjunctivas and nail beds were normally pink. (These were examined in particular because of the aforementioned anemia, the dark stools and the medicament which the patient was taking. The tablets were of the shape and color of some proprietary tablets containing ferrous sulfate.) The remainder of the physical examination gave negative results except for the following observations. The heart was enlarged to the left, the rate was 70, and the rhythm was regular. There was a rough apical murmur, which was not transmitted. The pulse was regular and of good volume. The abdomen was rounded but not distended. There were a scar over McBurney's point and one scar low in the midline, both of which were pink and firm. No hernias could be detected. The abdomen was soft throughout. In the right upper quadrant and toward the midline, tenderness was elicited on deep pressure. No masses could be palpated. Slight tenderness was elicited in the right costovertebral angle. No tenderness was present in the left angle.

The impression at this time was as follows. In view of the history of pnelitis six months previously, roughness of the throat and cervical adenitis one week previously, abdominal pain, urgency and frequency of urination and tenderness of the right upper quadrant of the abdomen and the right costovertebral angle at the time of examination it was felt that a recurrence of the renal infection was probably developing. In spite of the urgency and frequency of urination, a sample of the urine could not be obtained.

The patient was seen again at approximately 2 a. m. on January 15. The abdominal pain became more severe and shot across the upper part of the abdomen. At times the patient complained that it 'cut off her breath'. The urgency and frequency of urination persisted. The patient stated that there were no other symptoms. The temperature, pulse rate and respiratory rate were normal. The remainder of the physical examination gave results identical with those of the previous examination except that the tenderness in the upper middle part of the abdomen and in the right costovertebral angle was more marked.

About 7 a. m. on January 15, the patient was complaining of severe pain in the lower part of the abdomen which spread along the left side of the abdomen. The pain was much more severe than that complained of earlier in the evening. This sharp, severe pain in the lower part of the abdomen occurred suddenly about 6:30 a. m. and was followed by vomiting, the emesis containing neither old nor fresh blood. After the onset of the pain, the patient's family noticed a gradual change in her appearance. She was extremely pale, all color having disappeared from the skin, nail beds and conjunctivas. She was covered with cold perspiration. The pulse was rapid, and the volume was considerably less than on previous examinations. The abdomen was flat, and in both lower quadrants there was exquisite tenderness to moderate pressure. There was involuntary spasm but no rigidity. Examination of the pelvis revealed no fresh bleeding and no masses, but there was marked tenderness in both fornices, especially the left, and on motion of the cervix.

The patient was immediately taken to the hospital. On her arrival the pulse rate was 140 and the pulse was thready. The respiratory rate was 30. The blood pressure was 78 systolic and 58 diastolic. The color, the cold clammy skin and the abdominal signs were the same as before. The red blood cell count was 2,280,000 per cubic millimeter, the hemoglobin content was 48 per cent and the white cell count was 7,500. Intravenous administration of dextrose and saline solution was started immediately. Soon afterward the pulse rate dropped to 92, the volume improved and the blood pressure increased to 88 systolic and 68 diastolic. Suddenly the pulse again became rapid and thready. The patient sank rapidly and died before a transfusion could be given.

The clinical impression on the patient's admission to the hospital was, in addition to rheumatic endocarditis, "ruptured ectopic pregnancy." However, the subsequent course was much too rapid and severe for the latter, and it was felt that the patient had an exsanguinating intraperitoneal hemorrhage, the source of which was unknown.

Autopsy—General Observation The skin was extremely pale. Little blood was observed in the vessels.

Heart The heart weighed 310 Gm. The pericardial fat was preserved. The endocardium of the right atrium showed fatty patches. The tricuspid valve was thin and delicate. The wall of the right ventricle showed fatty infiltration. The mitral valve was thickened on its free margin. Along the line of closure of the anterior leaflet, especially where it joined the posterior leaflet, and along the line of closure of the posterior leaflet there were pinpoint-sized to pinhead-sized glistening gray vegetations. The larger of these were slightly polypous. The surfaces of a few were red. Recent hemorrhages were noted in the endocardium of the left ventricle. The myocardium was pale and showed patchy scarring. The aortic cusps showed small conglomerate vegetations in the noduli Arantii. The aorta measured 6 cm. above the valve. There was slight atheromatosis just above the sinuses, with pinhead-sized patches.

Lungs There were delicate fibrous bands running from the anterior surface of the upper lobe of the right lung to the parietal pleura. A few fibrous bands were present between the upper and the lower lobe. The interlobular fissure showed petechial hemorrhages. The mediastinal surface of the right lung was adherent to the mediastinum.

Peritoneal Cavity The peritoneum was bluish. When the cavity was opened, a large amount of fluid and clotted blood was found in the pelvis and in both subphrenic spaces. More than 2 quarts of blood was removed from the general peritoneal cavity. In the gastrohepatic ligament, along the lesser curvature of the stomach as far as the pylorus, but especially around and to the left of the celiac plexus, there was hemorrhage. The lesser sac contained free and clotted blood. Hemorrhage extended through the hiatus of the diaphragm surrounding the esophagus.

Splenic Artery The artery passed downward and slightly to the left for a distance of 2 cm., where it turned at almost right angles to the left. At this right angle turn opposite the origin of the splenic artery there was an aneurysm which could be measured only with difficulty. It was approximately 2.5 cm. in circumference. It was filled with laminated, somewhat soft mixed clot. This clot was adherent to the inner surface. The wall could not be followed with certainty around the whole aneurysm because of a rupture in the superior posterior part and also in the inferior part. The ruptured aneurysm pressed into the pancreas about 8 cm. from the tail. The pancreas at this point was atrophic. The horizontal course of the splenic artery was normal.

Spleen The capsule was wrinkled, and there was marked anemia. The organ measured 15 by 6 by 33 cm. The splenic vein was patent.

Stomach The stomach was contracted and compressed along the lesser curvature by the hemorrhage (fig. 2). The serosa was infiltrated with blood.

About 9 cm. from the cardiac orifice there was an indentation into the stomach at its lesser curvature and posterior wall measuring 33 by 2 by 15 cm., brought about by the aneurysm. The stomach was pushed down by the hemorrhage.

Abdominal Aorta The aorta showed slight atheromatosis.

Kidneys Each kidney measured 11.5 by 3.5 by 2.8 cm. The capsules were thin and stripped easily. Embryonal lobulations persisted. Both kidneys were

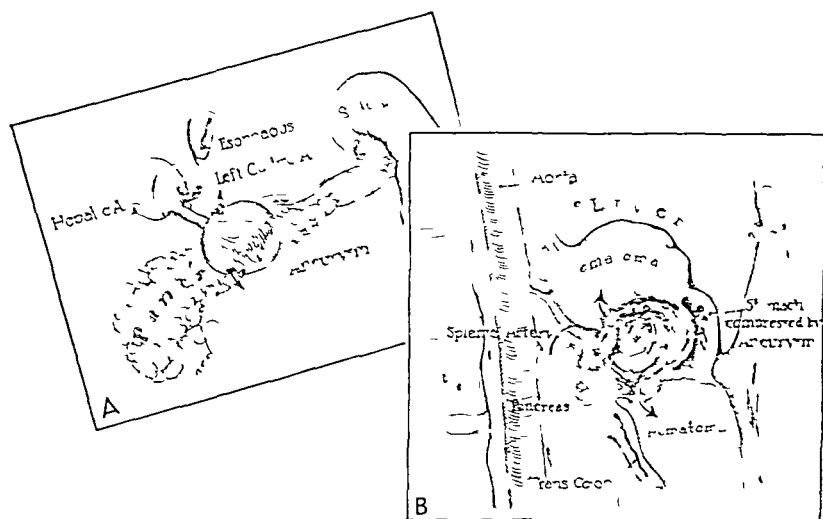


Fig 1—A, sketch showing the relative position of the aneurysm with the two sites of rupture B, sketch of the lateral view, showing the aneurysm, compression of the stomach superior and interior ruptures and sub-sequent hematomas

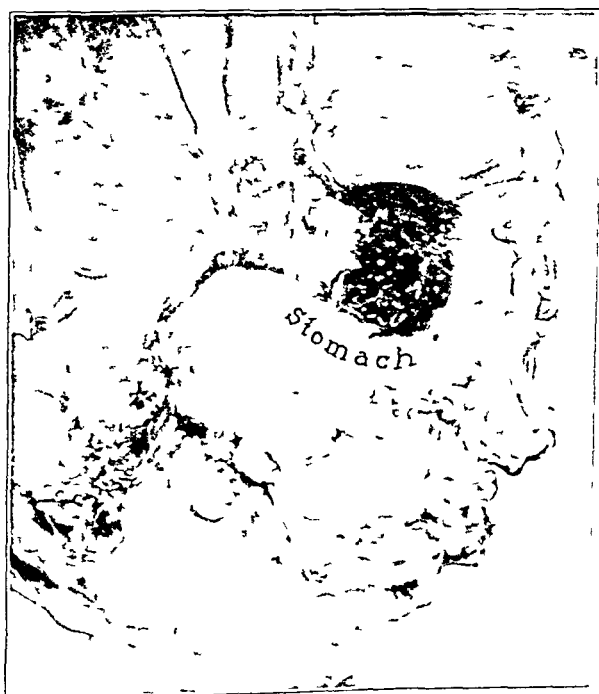


Fig 2—Liver lifted upward Note the dark glistening hematoma the gastrohepatic ligament pushing the stomach downward

very pale. The pelvis and ureters were normal. The left kidney showed a depressed scar which measured 1 by 0.5 cm.

Uterus. There were fibrous adhesions between the uterus and the pelvic peritoneum. There was a depressed scar in the midanterior surface, 2.5 cm in length and 1 cm from the superior margin. The continuity of the tubes was lost for the first 3.5 cm, but the preserved parts measured 8 cm and were normal.

The remainder of the postmortem examination gave essentially negative results except for marked anemia of all the viscera.

Pathologic Diagnosis.—The pathologic diagnosis was (1) ruptured aneurysm of the splenic artery 2 cm from the origin of the celiac axis, filled with laminated clot, (2) protrusion of the ruptured aneurysm into the wall of the stomach and into the pancreas, causing indentation into the stomach and atrophy of the pancreas, (3) hemorrhage into the serosa of the stomach and pancreas about the aneurysm, recent hemorrhage into the lesser sac, distinct hemorrhage into the gastrohepatic ligament, extension through the diaphragm about the lower end of the esophagus, (4) massive hemorrhage into the peritoneal cavity, with more than 2 quarts of fluid and clotted blood, (5) chronic rheumatic endocarditis of the mitral and aortic valves, with a number of firm gray vegetations, (6) petechial hemorrhages in the endocardium of the left ventricle, small patchy scarring of the myocardium in the posterior wall of the left ventricle, (7) fibrous bandlike pleurisy of the right lung to the parietal pleura and between the lobes, petechial hemorrhages in the right pleura, (8) depressed scar of the left kidney, probably following infarction, (9) marked softening and contraction of the spleen, with anemia, (10) slight atheromatosis of the abdominal aorta, and (11) status following an old cesarean section, with scar in the anterior wall of the uterus and ligation of the tubes, fibrous adhesions in the pelvis.

Chief Pathologic Diagnosis.—The chief pathologic diagnosis was ruptured aneurysm of the splenic artery with massive hemorrhage into the lesser sac and peritoneal cavity, generalized anemia.

Summary of Case.—The formation of the aneurysm may be attributed to an embolus arising from the heart valve. The depressed scarring of the left kidney may also be attributed to infarction arising from the same source, which was probably the so-called "pyelitis" of six months previous. There were no evidences of arteriosclerosis along the course of the splenic artery or in the wall of the aneurysm, although there was slight atheromatosis of the abdominal aorta. There was no evidence of syphilis. The lesion was of some duration, as was shown by indentation into the stomach, atrophy of the pancreas and lamination of the clot, but not long enough for calcification to have taken place.

Rupture probably occurred in two stages, the first starting as a slow leak about thirty-six hours before the patient was first examined. This was probably confined to the lesser sac and the gastrohepatic ligament. The second rupture, which gave rise to the massive, fatal hemorrhage, probably occurred about nine hours after the first examination, when the patient complained of sudden sharp pain followed by a definite change in appearance and condition.

Age and Sex Incidence—Aneurysm of the branches of the abdominal aorta is considered unusual. In 1928, Thompson¹ collected 65 cases of aneurysm of the hepatic artery, and Singer² collected 40 cases of aneurysm of the renal artery. In 1924 Baumgartner and Thomas³ collected 40 cases of aneurysm of the splenic artery. These cases represented the incidence in the previous fifty years, evidence of the fact that the condition is rare. In 1929, Anderson and Gray⁴ collected 58 cases of aneurysm of the splenic artery and reported an additional case. Their report included most of the 27 cases reported by Bertrand and Clavel⁵ in the same year. Since 1929, we have collected 24 additional cases and we report another in this paper. Lindboe⁶ collected pathologic reports made by Schroetter, Muller Bosdorf and Emmerich who altogether, in 41,437 autopsies observed 554 abdominal aneurysms of which only 21 were in the splenic artery, i. e. 0.05 per cent of the whole body material.

Most of the aneurysms occurred in the third decade of life. The aneurysms occurring in each of the fourth, fifth, sixth and seventh decades were almost as many. The difference in the numbers in different decades was not great enough to make the data on age incidence definite. In the reported cases in which the sex of the patient was stated the condition occurred twice as frequently in females as in males.

PATHOLOGIC PICTURE

The pathologic features of this lesion after rupture are difficult to interpret anatomically. In the upper part of the abdomen especially in the lesser sac, there is usually a poorly circumscribed mass of recent and organized clot with adhesion of the viscera. It is difficult to identify the lesion, and only after careful dissection can the various organs be separated. Bertrand and Clavel⁵ have made an extensive study of the pathologic picture and have compared the aneurysm to an inflammatory tumor, which has created all around itself multiple and thick adhesions to all the organs of the region, namely the stomach (posterior surface) pancreas, colon and spleen.

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5 Bertrand, P., and Clavel, C. La rupture des anévrysmes de l'artère splénique. Lyon chir. **26** 641 1929.

6 Lindboe, E. F. Aneurysm of the Splenic Artery Diagnosed by X-Ray and Operated upon with Success. Acta chir. Scandinav. **72** 108 1932.

Twenty-Five Cases of Aneurysm of the Splenic Artery

Case No	Author and Reference	Age, Sex	Comment	Physical Examination	Preoperative Diagnosis	Treatment	Recovery	Pathologic Picture
1	Brockman 21	69 F	Violent pain in left upper quadrant, vomited, desire to defecate, no result with enema	Shock, bruit in left upper quadrant, temperature 91°, pulse 120	Ruptured splenic aneurysm (?), acute intestinal obstruction	Splenectomy	Recovery	Marked hemorrhage from splenic pedicle, vessels and structures ploughed up by hemorrhage
2	Brockman 21	? M	Acute abdominal pain, treated expectantly and improved, two weeks later seized with severe pain, vomited, passed blood by bowel and died suddenly	None recorded	None recorded	Rest, morphine	Death	Aneurysm of splenic artery, ruptured secondarily into large bowel
3	Wacker, Baumgartner, Ronnau and Gadicke 28	40 F	Repeated violent hemiplegic coma relieved with insulin	Mass in left hypochondrium, marked asthenia	Round calcified area in spleen	Splenectomy	Recovery	Two large saccular aneurysms partially calcified and with small dilatations more or less aneurysm like on the branchings of the artery
4	Rocker, P. Beitrage zur hamorrhagischen Milznektomie in die Bauchhöhle infolge einer A. lienalis, Zentralbl f Chir 15, 1911	70 M	Operated on for adenocarcinoma of stomach, 4th postoperative day sudden pain left shoulder temperature and pulse rate normal, relief with enema, 5th postoperative day it tempted to sit up, sudden collapse and death	None recorded	Pulmonary embolus	None for lesion of splenic artery	Death	Aneurysm 3 cm from splenic hilum with fibrous tissue and calcification hemorrhagic necrosis and rupture of spleen subsequent to postoperative thrombus
5	Lower and Larrick 2	16 M	Paroxysms of severe abdominal pain for 8 years,arry phic onset relief with morphine cough	Pale and undernourished, formity and hypermotility of duodenum	Chronic pancreatitis	Removal of tumor with part of tail of pancreas	Recovery	Aneurysm of splenic artery, fibrosis of glandular pancreatic tissue
6	Luthcke 29	53 M	Epigastric pain dyspepsia lassitude	Anemic, undernourished, pale and thin	Calcified aneurysm of splenic artery	Splenectomy with removal of aneurysm	Recovery	Aneurysm of splenic artery with hyaline degeneration and calcification
7	Mohr 30	67 M	Mild "stomach ache" sharp severe pain left hypochondrium condition worse 3 days later signs of internal hemorrhage	Pale anuric fainting spells systolic blood pressure 90 large mass in left upper quadrant dull to percussion noticeable pulsation and murmur	Ruptured aneurysm of splenic artery	Splenectomy, removal of aneurysm and portion of tail of pancreas	Death	Hemorrhage only into retroperitoneal space aneurysm of splenic artery 6 cm from spleen ruptured posteriorly

9	Infante J. O. Sobre un caso de falso aneurisma de la arteria esplénica. Rev. Soc. Argent. de Biol. 8: 133, 1932	22	Pain in right wrist 2 weeks, few days later severe pain localized in left hypochondrium and groin	None recorded	None recorded	Hemorrhagic peritonitis with possible perforation of the uterus	Exploration source of bleeding not determined	Death	I also aneurysm of splenic artery because part of wall of artery was missing and faint infarct of spleen
9	Hefelkamp	?	Light monthly precursus, no prodromal symptoms, sudden and acute onset	None recorded	None recorded	None recorded	Died before hospitalization	Death	Massive hemorrhage, ruptured splenic aneurysm, septically possibly mycotic 1 cm from hilus
10	Levy and Little	78 M	Sudden nonradiating epigastric pain, enlarged spleen for 3 years, hypertension	Acutely ill, anemic blood pressure 108/52, pulsating, lemon sized mass in left upper quadrant, bruit enlarged spleen	Aneurysm of abdominal aorta, splenomegaly, bilateral inkblot hernia	Supportive no operation	Death	Abdomen full of blood, ruptured aneurysm of splenic artery patches of calcification present	
11	Remmow	71	Colicky abdominal pain and bloody stools	Tenderness of left side of abdomen, tumor palpated under left costal arch	Dysentery, chronic ulcerative colitis	Splenectomy and removal of aneurysm	Death	Aneurysm in hilar region of enlarged spleen, thrombi in splenic veins	
12	Levy and Spitzer	40	Sudden severe epigastric pain, right shoulder pain, vomiting, full term pregnancy	Cyanotic, shallow respiration, uterus not contracting, tenderness of epigastrium, no shock	Ruptured viscera	Low cervical cesarean section	Death	Massive abdominal hemorrhage, ruptured splenic aneurysm, sclerosed intima	
13	Rupture of an aneurysm of the Splenic Artery. Canad. Jour. Med. Sci. 1931	41	Twelve hours before admission sudden upper abdominal pain and collapse, vomited 15 times during night	Low blood pressure on admission, acute distention, ascended abdomen tender lower quadrants, especially the left	None recorded	Exploratory laparotomy	Death	Massive abdominal hemorrhage, ruptured aneurysm of splenic artery about 1.5 cm in diameter as it passes through tail of pancreas	
14	Goertzel	43	Intermittent colicky pain in right upper quadrant radiating to right shoulder epigastric fullness, nausea and occasional vomiting 27 years, explored	Slight tenderness in right upper quadrant, gall bladder normal to routine examination	Cholecystitis with stones	Exploration, clamping aneurysmal necks, ligation in situ	Death	Aneurysm of splenic artery with calcification and laminated clot, gallbladder normal	
15	Prism M. Das. Röntgenbild der verkrampften Milzarterie und eines verkrampften Arterien der Milzarterie. Röntgenpraxis 8: 140, 1936	71	Nonformable to splenic artery	None recorded	Impyema of gall bladder, multiple liver abscesses	None directed to splenic lesion (condition discovered at autopsy)	Death	Cherry sized aneurysm in center of splenic artery with thick calcified walls	
16	Reinhardt, M. A. et al. of Splenic aneurysm with Aneurysm of the Splenic Artery. Arch. Surg. 1936	41	Diffuse vague abdominal discomfort for 10 years, pain worse when standing	Sensitive in epigastrium	Calcified aneurysm of splenic artery	Splenectomy and removal of aneurysm	Recovery	Aneurysm of splenic artery at hilus of spleen 2 by 1.6 cm, wall calcified, descending changes in the artery	
17	Reinhardt, M. A. et al. of Splenic aneurysm with Aneurysm of the Splenic Artery. Arch. Surg. 1936	?	Original article not seen					Aneurysm of splenic artery splenomegaly	

Twenty-Five Cases of Aneurysm of the Splenic Artery—Continued

Case No	Author and Reference	Age, Sex	Comment	Physical Examination	Preoperative Diagnosis	Treatment	Result	Pathologic Picture
18	Safwenberg 7	66 F	None referable to splenic lesion	Signs referable to urinary tract	Carcinoma of bladder, aneurysm of splenic artery	None directed to splenic artery (condition discovered at autopsy)	Death	Aneurysm of bladder 2 1/2 by 1 1/2 cm and 1 1/2 by 0.5 cm spleen not enlarged
19	Safwenberg 7	68 F	Fatigue, bad appetite, loss of weight	Signs referable to urinary tract	Polycystic kidney, aneurysm of splenic artery	None directed to splenic artery (condition discovered at autopsy)	Death	Calcification of splenic artery, two aneurysms about 1 cm in diameter
20	Parsons 20 (October 1934)	45 M	Cramplike epigastric pain, shoulder pain, improved in 5 days, recurrence 6th day and hospitalized	Shock, abdomen distended, rigid and tender, especially left lumbar region	Perforated gastric ulcer	Splenectomy and removal of aneurysm	Recovery	Aneurysm of splenic artery fibrous hyaline degeneration of vessels
21	Parsons 20 (same patient August 1936)	47 M	Severe upper abdominal pain, vomiting, re-admitted	Shock, distended abdomen, tender left upper quadrant, dull in left loin	"Picture of a woman bleeding from ruptured ectopic gestation"	Cavity of aneurysm packed	Death	Massive hemorrhage ruptured aneurysm of splenic artery prox to point of removal in first operation
22	Cady 8	50 F	None referable to splenic aneurysms	Acutely ill owing to wide spread infection arising from other source, splenomegaly	Common duct obstruction aneurysms seen at autopsy	None directed to splenic lesion	Death from acute infection	Seven aneurysms of the splenic artery, the largest 8 cm and the smallest 1.5 cm in diameter, calcification in walls
23	Schnitzer 11	62 F	None referable to splenic aneurysm	Picture of congestive heart failure, severe anemia, familial hemorrhagic telangiectasis	Gastric ulcer, aneurysm of splenic artery	None directed to splenic aneurysm	Death from broncho pneumonia	Three aneurysms of splenic artery with calcified walls, internal elasticity of media and congenital
24	Lucas 9	60 M	Pain in upper part of abdomen, vomiting, constipation in last 2 months	Shock, marked pallor, exquisite tenderness and spasm in lower part of abdomen	Rheumatic heart disease ruptured ectopic pregnancy on admission but subsequent course was much too severe to suggest intrabdominal hemorrhage source unknown	Not recorded	Not stated	No confirmation of roentgen diagnosis reported
25	Mahomed and Lucas (present paper)	70 F	Mild upper abdominal pain more severe especially in lower part of abdomen				Death	Aneurysm of splenic artery rupture in superior and inferior part filled with soft laminated mixed clot

The aneurysmal wall is usually thickened, surrounded by old clot in which it is difficult to find the fissure or rupture. The rupture itself is variable in size and location, ranging from a small punched-out area to an irregularly torn rip. In some instances considerable quantities of calcification are observed within the wall of the sac, while in others, as in our case, no calcification is present.

The splenic artery in some instances has been involved in generalized atherosclerosis, as described by Säfwenberg.⁷ In Cadé's case⁸ the atherosclerosis was localized to the splenic artery. In Lindboe's case⁶ fibrous degeneration was present, while in Sered and Steiner's⁹ and LeFevre and Pettis'¹⁰ cases sclerosis and calcification were present only in the media of the splenic artery.

In Schuster's case¹¹ the main trunk of the splenic artery showed a fine fibrosis and loss of elastic tissue of the media. In a secondary branch there was reduplication of the internal elastic lamina, while in the tertiary branch there was a complete deficiency of the media over the point of the cleft.

In 12 of the 27 cases reported by Bertrand and Clavel¹ the spleen was hypertrophied. Remizov¹² reported the presence of splenomegaly in about 50 per cent of cases of aneurysm of the splenic artery. Microscopic examination of the spleen showed only chronic passive congestion of the splenic parenchyma. In LeFevre and Pettis' case¹⁰ splenomegaly was diagnosed three years prior to the occurrence of fatal hemorrhage from the ruptured splenic aneurysm.

ETIOLOGY

In this review, as in others, it seems impossible to mention an outstanding causative factor. Aside from varying degrees of calcification found in the wall of the aneurysm, atheromatous changes are most frequently seen in microscopic examination of the artery. Syphilis is said to be an etiologic factor, but in none of our cases was it present. In 6 cases of the series reported by Baumgartner and Thomas³ it was mentioned particularly that there was no history of syphilis, and the

7 Säfwenberg, O. Zwei röntgenologisch diagnostizierte Fälle von Milzarterienaneurysma, *Acta radiol.* **18** 481, 1937.

8 Cadé, J. B. Aneurysm of the Splenic Artery, *Guthrie Clin. Bull.* **6** 145 1937.

9 Sered, H., and Steiner, L. M. Full Term Pregnancy Complicated by Ruptured Splenic Aneurysm, *Am. J. Obst. & Gynec.* **29** 606 1935.

10 LeFevre, G. L., and Pettis, E. M. Aneurysm of Splenic Artery with Fatal Hemorrhage, *J. Michigan M. Soc.* **34** 358, 1935.

11 Schuster, N. H. Familial Hemorrhagic Telangiectasia Associated with Multiple Aneurysms, *J. Path. & Bact.* **44** 29, 1937.

12 Remizov, A. A. Saccular Aneurysm of the Splenic Artery, *Soviet Med.* 1935, no. 8, p. 136.

findings and Wassermann reaction were negative. Binder¹³ stated that syphilis is not a factor except in aneurysm of the aorta. Chronic infection and direct or indirect trauma have been considered etiologic factors in reported cases because symptoms shortly followed the infection or trauma.

Ponfick¹⁴ stated that endocarditis is one of the main factors responsible for aneurysm of the splenic artery. He expressed the opinion that for the production of an aneurysm there must be an embolism at the branching of a vessel which lies in loose supporting tissue.

Tarrozzi¹⁵ described an aneurysm of the splenic artery and noted the lack of elastic membrane. He thought that localized collections of elastic tissue with intervening areas without this tissue might be a causative factor.

In the splenic aneurysm described by Schuster¹¹ the internal elastic lamina showed short lengths of reduplication into poorly stained strands, which entirely disappeared in certain places. In one area there was a complete deficiency of the media, the gap being filled with connective and elastic tissue of the adventitia. Schuster stated that aneurysm of the splenic artery may be another manifestation of inborn vascular defects. Other arterial systems are subject to the same hazard of multiple aneurysmal dilatations, notably the cerebral, hepatic, renal and coronary arteries. In series of cases of aneurysm of these arterial systems, he stated, there are certain inexplicable cases in which the aneurysm might be regarded as having a congenital basis. The original suggestion he attributed to Eppinger¹⁶.

Selter¹⁷ stated the opinion that increased blood pressure following embolism is essential to the formation of an aneurysm. Rolleston¹⁸ added that a weakened vessel wall in addition to increased pressure is necessary for formation of an aneurysm. Remizov,¹² in a sense,

13 Binder, V. Aneurysm der Arteria lienalis mit todlicher Blutung, Verhandl d deutsch path Gesellsch **16** 225, 1913.

14 Ponfick. Ueber embolische Aneurysmen, nebst Bemerkungen über das acute Herzaneurysma (Herzgeschwür), Virchows Arch f path Anat **58** 528, 1873.

15 Tarrozzi, G. Ein echten Aneurysma der Milzarterie, Centralbl f allg Path u path Anat **15** 700, 1904.

16 Eppinger, H. Pathogenesis (Histogenesis und Aetologie) der Aneurysmen einschliesslich des Aneurysma equi verminosum, Arch f klin Chir (suppl) **35** 1, 1887.

17 Selter, P. Ein Aneurysma der Milzarterie, entstanden in Folge einer durch Embolie hervorgerufenen Blutdrucksteigerung, Virchows Arch f path Anat **134** 189, 1893.

18 Rolleston, F. Aneurysm of the Splenic Artery, Tr Path Soc Lond **50** 55, 1898.

combined these two ideas in stating that there are two main factors in the development of an aneurysm of the splenic artery, preliminary degeneration of the arterial wall and a consequent or concomitant rise of blood pressure. In his case old thrombi were present in the splenic vein, which suggested stasis in the splenic circulation and increased pressure in the splenic artery.

While reviewing these various conceptions it is interesting to note that 8 cases¹⁹ of aneurysm of the splenic artery have been reported in which the condition appeared as a complication of pregnancy. In all cases it appeared during the eighth and ninth months or during labor. The condition was usually diagnosed as ruptured viscus. In all cases it proved to be a fatal complication of the pregnancy.

CLINICAL ASPECTS

In reviewing the clinical picture of reported cases, it is readily apparent that the greatest obstacle to diagnosis is the absence of a definite clinical picture. In the case reported by Parsons²⁰ the symptoms closely simulated those of gastric ulcer and perforation. In Osborne's case²¹ the picture was that of cholecystitis with cholelithiasis. In Lower and Farrell's case²² the clinical picture and findings were those of chronic pancreatitis. The pressure of the aneurysm caused extensive fibrosis of the glandular tissue, producing an external secretory deficiency although the islet tissue remained intact. In many instances there was no history to suggest the presence of an abdominal lesion until hemorrhage occurred. Repeatedly in the female the diagnosis of "ruptured ectopic pregnancy" was made. In a few cases the lesion produced no symptoms and was found incidentally at autopsy.

19 Wesenberg W. Verblutung während der Geburt inolge Ruptur einer Aneurysmas der Milzarterie. *Zentralbl. f. Gynäk.* **36** 463 1912. Van Rooy A. H. M. J. Rupture of Splenic Aneurysm at End of Pregnancy. *Nederl. maandschr. v. geneesk.* **14** 507 1927. Lundwall K. and Godl A. Aneurysm of Splenic Artery Ruptured at the Ninth Month of Pregnancy with Fatal Hemorrhage. *Arch. f. Gynäk.* **113** 177 1923. Saenger H. Fatal Hemorrhage in the Eighth Month of Pregnancy from Rupture of Aneurysm of Splenic Artery. *Zentralbl. f. Gynäk.* **50** 1324 1926. Mayer E. Verblutung nach der Geburt inolge Ruptur eines Aneurysmas der Arteria lienalis. *ibid.* **52** 754 1928. Remmelts E. Case of Sudden Death During Pregnancy from Rupture of Aneurysm of the Splenic Artery. *Tijdschr. v. prakt. verlosk.* **32** 126 1928. Heuveldop. Ein Fall von Ruptur eines Aneurysmas der Milzarterie. *Centralbl. f. allg. Path. u. anat.* **61** 277 1934. Scred and Steiner.⁹

20 Parsons C. G. A Case of Ruptured Aneurysm of the Splenic Artery with Recurrence. *Brit. J. Surg.* **24** 708 1937.

21 Osborne S. F. Aneurysm of the Splenic Artery Simulating Cholecystitis. *Lancet* **1** 1007 1936.

22 Lower W. E. and Farrell J. I. Aneurysm of the Splenic Artery. Report of a Case and Review of the Literature. *Arch. Surg.* **23** 182 (Abstr.) 1921.

Aneurysm of the splenic artery may be considered a symptomless lesion until its effect on neighboring viscera or surrounding structures is manifest or until rupture occurs. Pain is the most common symptom at the onset and is usually located in the epigastrium. It is usually mild and may be colicky, although other types have been described. Parsons²⁰ stated that the pain of gastric ulcer is probably due to severe spasm of the muscular wall of the stomach. In his case the aneurysm was adherent to the lesser curvature of the stomach, and it is possible that by irritation it produced a similar type of spasm. Dyspepsia, weakness, lassitude, nausea and vomiting were occasionally present in the reported cases. In some cases there was an enlargement of the spleen or a mass was palpable in the upper part of the abdomen. Occasionally a pulsation was felt or a bruit was heard in the upper part of the abdomen. At the time when extensive rupture and massive hemorrhage occur there is violent pain quite different from the pain at onset.

Brockman²³ pointed out that rupture of the aneurysm takes place in two stages. The first rupture occurs in the lesser sac, producing mild peritonitis with subsequent formation of adhesions. The primary rupture is usually not fatal, since clotting in the more or less closed space of the lesser sac occurs in a short time. At some later time a secondary rupture occurs, with severe internal hemorrhage, this usually terminates fatally. In most cases the aneurysm ruptures secondarily into the abdominal cavity, although it has been known to rupture into the stomach, the colon, the stomach and colon, the stomach and abdominal cavity or (once) the splenic vein.

Bertrand and Clavel⁵ expressed the opinion that the rupture occurs progressively. The wall of the aneurysmal pocket becomes fissured, creating all around it a hematoma, which tends to become organized, thus creating new adhesions. The first hemorrhage, therefore, occurs usually in a mass of adhesions, which tends to limit it. Bertrand and Clavel expressed the opinion that the evolutionary character of the entire aneurysmal and perianeurysmal mass determines the clinical aspects and contributes to the difficulty of diagnosis.

The clinical picture after secondary rupture is that of an acute condition of the abdomen. It may simulate and has been diagnosed as perforated gastric ulcer, acute intestinal obstruction, acute pancreatitis, pulmonary embolism, mesenteric thrombosis, ruptured ectopic gestation or ruptured viscus in pregnancy. The final clinical picture has usually been that of severe internal hemorrhage.

²³ Brockman, R. St. L. Aneurysm of the Splenic Artery, *Brit J Surg* 17: 692, 1930.

DIAGNOSIS

As has been stated, the diagnosis has rarely been made before operation. Hogler²⁴ has in 2 cases diagnosed aneurysm of the splenic artery on the basis of a systolic murmur over the hilus of the spleen. In both cases the diagnosis was verified at autopsy. Brockman²⁵ heard a bruit in the left upper quadrant of the abdomen which suggested to him an aneurysm of the splenic artery, but because of the clinical picture he felt that the condition was acute intestinal obstruction. Brockman stressed the value of abdominal auscultation in diagnosis of this lesion. Mallet-Guy²⁵ found a large mass in the left upper quadrant of the abdomen, which was dull to percussion and had a noticeable pulsation. A murmur was heard over the mass, and a diagnosis of ruptured aneurysm of the splenic artery was made. The diagnosis was confirmed by operation.

Lindboe⁶ reported a case in which symptoms caused the patient to seek aid before rupture occurred and the diagnosis was made by roentgen examination. A sharply defined calcareous ring was found behind the stomach. Repeated roentgen examinations ruled out an aneurysm of the adjacent arteries, principally the renal and gastric sinistra. The diagnosis of aneurysm of the splenic artery was confirmed by operation.

Haffner²⁶ reported 1 case and Säfwenberg⁷ 2 cases in which the condition was diagnosed by the roentgen findings. Round, irregular shadows of calcification were seen in the left upper quadrant of the abdomen. The calcareous areas were proved to be outside of the stomach and the kidney. The shadows moved on respiration and were less dense in the center. Haffner's diagnosis was confirmed by operation, and Säfwenberg's diagnoses were confirmed by autopsy.

Israelski²⁷ described a case in which a twisted shadow with double contour was seen with the aid of the roentgen rays. The diagnosis, although suggested, was not definitely made until autopsy, when a calcified splenic artery with cylindric dilatation of the middle part was found.

24 Hogler, F. Beitrag zur Klinik des Leber- und Milzarterienaneurysmas. Wien Arch f inn Med **1** 509 1920.

25 Mallet-Guy, P. Aneurisme de l'artere splénique rompu dans l'arruercavité des épiploons et le tissu cellulaire rétroperitonéal. Arch franco belges de chir **33** 1064 1932.

26 Haffner, I. Fall von verkalktem Aneurysma der Art lienalis. Acta radiol **17** 602 1936.

27 Israelski, M. Die verkalkte Arteria lienalis im Röntgenbilde. Röntgen praxis **2** 670 1930.

Trvier, Baumgartner, Ronneux and Gadreau²⁸ reported a case in which a shadow was seen on roentgen examination but a definite diagnosis was not made until operation. The difficulty they encountered in diagnosis was attributed to a 90 degree rotation of the spleen on its vertical axis, which cast the shadow in the position of the splenic parenchyma.

Fuchs²⁹ reported a case of aneurysm of the splenic artery in which the lesion was diagnosed by roentgen examination. There was a walnut-sized shadow of calcification below the left side of the diaphragm, near the midline, which moved with the diaphragm. No confirmation of the diagnosis, however, is reported.

PROGNOSIS AND TREATMENT

Lower and Farrell²² collected from the literature 15 cases in which some surgical procedure was attempted. Seven of the patients recovered, an operative mortality of 53 per cent. In 4 cases a tampon was used to control the bleeding, and all the patients died. In 1 successful case the large vessels entering and leaving the aneurysm were ligated. All other successes followed removal of the aneurysm, the spleen and, in 2 instances, a portion of the adjacent pancreas.

In the series reported here, 18 patients died, a general mortality of 75 per cent. Thirteen of the patients were operated on, and 7 died, an operative mortality of 47 per cent. However, in only 8 of the 13 operative cases was an attempt made to remove the aneurysm and the spleen or to ligate the vessels. In this group of 8 cases, 2 patients died, an operative mortality of 25 per cent. In the other unsuccessful cases, such procedures as packing the cavity, clamping the sac and simple exploration were done.

Obviously the treatment of this lesion is entirely surgical, although the exact diagnosis of its type and location cannot always be made before operation. The ideal treatment consists of removing the aneurysm, the spleen and, if need be, the adjacent pancreas. The value of heat, morphine, fluids and adequate transfusion should not be overlooked. Packing the marsupialized cavity and clamping the sac are only palliative procedures, which at the moment may save the patient, but require further surgical procedures for a permanent cure.

Dr. Samuel Sanes of the Department of Pathology furnished the pathologic description in the case presented.

²⁸ Trvier, Baumgartner, Ronneux and Gadreau. *Aneurismes calcifiés de l'artère splénique et splénomégalie*, Bull. et mem. Soc. de radiol. méd. de France 18: 349, 1930.

²⁹ Fuchs, G. *Das Röntgenbild des Aneurysmas der Arteria lienaris*. Roentgenpraxis 9: 467, 1937.

HYPERFUNCTIONING ADENOMA OF AN ECTOPIC PARATHYROID GLAND

REPORT OF A CASE

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AND

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DETROIT

HISTORICAL CONSIDERATIONS

The parathyroid glands, which are derived from the third and fourth branchial clefts,¹ were first recognized and named by Sandstrom in 1880. A parathyroid tumor was first recognized by de Santi in 1900. Gradually the relation between such a tumor and the syndrome of von Recklinghausen's disease was realized, and in 1925 Mandl² reported the cure of the latter by removal of an enlarged parathyroid gland. Since then, reports of about 200 cases have been added to the medical literature.

ANATOMY

The parathyroid glands are present in all animals down to fishes. They may be situated on, in or behind the thyroid gland but are most frequently found on its posterior aspect, near the point at which the inferior thyroid artery enters the gland.³ Rarely, aberrant or accessory parathyroid glands have been reported as present in the thymus or in the anterior mediastinum.⁴ Millzner⁵ has frequently found parathyroid glands on the anterior surface of the thyroid, but Gilmour¹ found only two anteriorly situated in 428 dissections. Four parathyroid glands are usually present, but careful search sometimes reveals only three or even two. Gilmour found an average of four parathyroids in each subject but actually found four in 87 per cent, two in 0.2 per cent, three in 6.1 per cent, five in 6 per cent and six in 0.5 per cent. More, up to

1 Gilmour, J. R. The Gross Anatomy of the Parathyroid Glands. *J. Path. & Bact.* **46**: 133, 1938.

2 Mandl, F. Klinisches und Experimentelles zur Fragen der lokalisierten und generalisierten Ostitis fibrosa. *Arch. f. klin. Chir.* **143**: 245, 1926.

3 Lahey, F. H., and Haggard, G. E. Hyperparathyroidism. *Surg., Gynec. & Obst.* **60**: 1033, 1935.

4 Hunter, D., and Turnbull, H. M. Hyperparathyroidism: Generalized Osteitis Fibrosa with Observations upon Pioneering Parathyroid Tumor and Normal Parathyroid Glands. *Brit. J. Surg.* **19**: 203, 1931.

5 Millzner, R. I. The Occurrence of Parathyroids on the Anterior Surface of the Thyroid Gland. *J. A. M. A.* **88**: 1053 (April 2), 1927.

eleven and twelve, have been reported, but there is some doubt as to the accuracy of the reports.¹ The parathyroids are shaped like lima beans. They are reddish or light brown. Their maximum size is 8 mm in length by 4 mm in width.

PATHOLOGY

Hyperparathyroidism is a disease due to hyperplasia of the parathyroid parenchyma or to the presence of a hyperfunctioning adenoma resulting in increased secretory activity of the gland.⁶ In diffuse hyperplasia only a portion of one gland (rarely, portions of two glands) may be involved.

Adenomas of the parathyroid glands are smooth and firm. They are round or ovoid and may vary greatly in size. As a rule they are small, being rarely palpable. Sometimes they are not more than twice the size of a normal gland and yet produce symptoms. Growths have been reported, however, which weighed 300 Gm or more. The most typical cell of such neoplasms is a large clear or vacuolated cell, the *wasserhelle* cell, which is similar to the typical clear cell of hypernephroma. Smaller, acidophilic cells also may be present.^{6a} Hyperparathyroidism is due to hyperfunctioning adenoma seven or eight times as frequently as to hyperplasia.

The secretory hyperactivity of the gland produces a calcium-phosphorus imbalance, causes migration of calcium from bone and results in hypercalcemia. Calcium and phosphorus in the blood are subject to the laws of ionic dissociation, that is, the concentration of calcium ions and that of phosphate ions if altered must vary inversely with each other in order that they may remain in equilibrium with the amount of undissolved calcium phosphate.⁷ The first action of the parathyroid hormone is to sweep phosphates from the blood into the urine. The phosphate content of the serum then falls, and consequently the calcium content rises. The excess of calcium is secreted by the kidneys, and the reserves of both calcium and phosphate are mobilized from bone. The loss of calcium salts from bone produces a lesion of the skeletal system known as osteitis fibrosa cystica or von Recklinghausen's disease.

The osseous changes consist of decalcification, the formation of degenerative cysts, hemorrhagic extravasation and replacement of the decalcified bone by connective tissue containing numerous giant cells of the osteoclastic type. These giant cells may be fused phagocytes the function of which is to remove osseous debris. Pathologic fractures are common. Hemorrhage is part of the picture of active decalcification.

⁶ Castleman, B., and Mallory, T. B. The Parathyroids in Hyperparathyroidism, *Am J Path* **11** 1, 1935.

^{6a} Warren, S., and Morgan, J. R. E. The Parathyroid Gland. A Histologic Study of Parathyroid Adenoma, *Arch Path* **20** 823 (Dec) 1935.

⁷ Taylor, H. Osteitis Fibrosa. An Experimental Study, *Brit J* **5** 22 561, 1935.

because the high concentration of calcium damages the vascular endothelium. Hemorrhage interferes with healing.

Because of hypercalcemia the calcium concentration of the urine is increased and the formation of urinary calculi is a prominent part of the disease. Uremia may result from impaction of the renal pelvis with crystals of calcium phosphate.⁸ A case in which death occurred from such uremia was observed by one of us (O. A. B.).

CLINICAL FEATURES

Hyperparathyroidism occurs two and one-half times as frequently in females as in males. While cases have been reported in which the condition occurred from the second to the ninth decade, in about half of

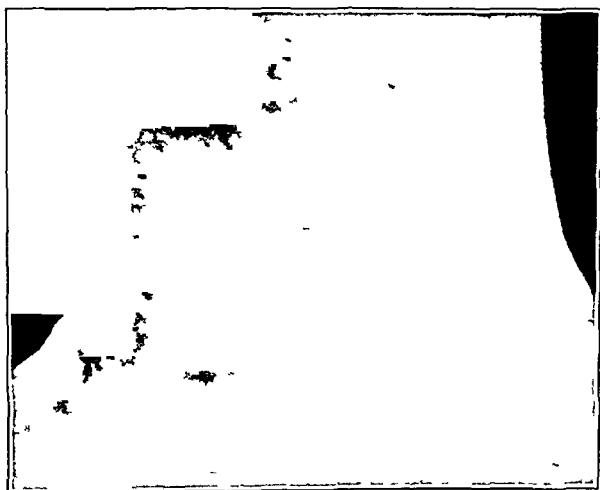


Fig. 1—Operative scar, indicating the site of the tumor.

all cases it occurs in persons between 40 and 60 years of age. In only 6 per cent of reported cases has it occurred in the second decade.

Clinical symptoms^{8a} usually consist of pain and localized swelling of bone, possibly with deformity and disturbance of gait. Nephrolithiasis and associated renal infection may lead to abdominal symptoms sometimes diagnosed as duodenal ulcer or appendicitis. Polyuria and polydipsia may be present. Terminally the patient may lose height owing to destruction of the skeletal system. However, hyperparathyroidism is

⁸ Elson K. A., Wood F. C., and Ravdin I. S. Hyperparathyroidism with Renal Insufficiency. *Am J Med Sci* **191**: 49, 1936.

^{8a} Gutman, A. B., Swenson, P. C., and Parsons W. B. Differential Diagnosis of Hyperparathyroidism. *J. A. M. A.* **103**: 87 (July 14) 1934.

not necessarily associated with osseous changes. Many patients with hyperparathyroidism have no symptoms referable to the skeletal system and present no roentgen evidence of disease of bone. There may be no elevation of the phosphatase content of the blood and no evidence of osseous changes at biopsy.⁹

It is generally understood that the disease is characterized by a high calcium and a low phosphorus content of the serum. Shelling¹⁰ stated that the lower limit of the value for serum calcium in cases of hyperparathyroidism is 12.5 mg per hundred cubic centimeters. However, Albright and his associates⁹ stated that the average value for serum calcium was below 12.5 mg in 40 per cent of their 35 cases, the lowest average being 10.7 mg. Chemical examination of the urine reveals a high urinary output of calcium, and the total protein content of the serum is low.

Roentgen findings consist of osteoporosis and the presence of cysts.¹¹ The calvarium may be thickened and granular and the tables of the skull indistinct. The cortex of the long bones may be thin, indistinct and irregular. All the bones may be involved. Renal calculi may be demonstrated.

In the differential diagnosis of the osseous lesions associated with hyperparathyroidism the following diseases must be considered:

- Focal osteitis fibrosa
- Metastatic carcinoma
- Multiple myeloma
- Osteogenesis imperfecta
- Single bone cyst
- Senile osteoporosis
- Paget's disease
- Osteomalacia

Space does not permit a detailed discussion of the differential diagnosis. The reader is referred to the recent literature.

TREATMENT

Surgical removal of the adenoma or the involved gland results in immediate correction of the disturbance in calcium-phosphorus metabolism.

9 Albright, F., Sulkowitch, H. W., and Bloomberg, E. Further Experience in Diagnosis of Hyperparathyroidism, *Am J M Sc* **193** 800, 1937.

10 Shelling, D. H. The Parathyroids in Health and Disease, St. Louis C. V. Mosby Company, 1935.

11 Camp, J. D. Osseous Changes in Hyperparathyroidism. A Roentgenologic Study, *J A M A* **99** 1913 (Dec. 3) 1932.

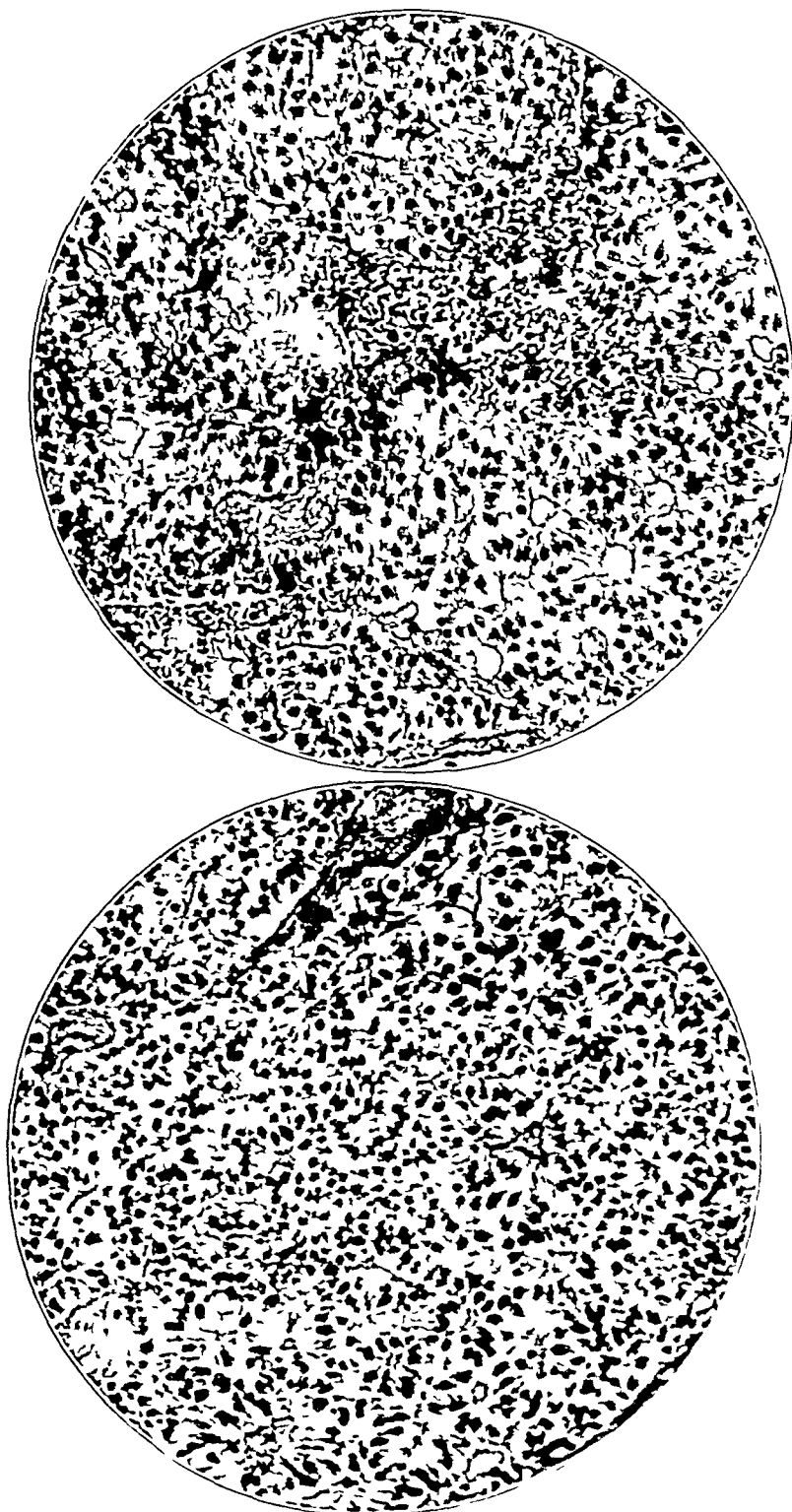


Fig. 2—Photomicrographs representing two different portions of the adrenal.

lism. Improvement in many symptoms usually follows. If the disease is in an early stage and the osseous changes are mild, a complete return to normal structurally may be expected. In cases of more advanced involvement repair of bone occurs slowly, and in cases of far advanced involvement complete recovery cannot be expected. Immediate symptomatic and structural improvement is impressive, but the results are not necessarily permanent. Location of the adenoma or hyperplastic gland at operation is not always easy, and multiple operations have been necessary, 1 case having been reported in which the adenoma was found at the seventh operation.¹² Recurrence of symptoms due to the formation of other adenomas or to hyperplasia occurring in remaining glands have been reported, necessitating reoperation. Other cases have not been followed for long periods. Roentgen therapy may decrease the activity of the gland, but experience with this form of treatment has been limited.¹³ Administration of calcium, phosphorus and vitamin D has been advocated.¹⁴

REPORT OF A CASE

M. S., an 18 year old white girl, was first seen in the office of one of us (V. L. B.) on Feb. 1, 1936, complaining of recurrent pain in the right lower quadrant of the abdomen and of two tender nodules in the right anterior triangle of the neck. Neither complaint was disabling, and she appeared for examination because her sister had recently had a ruptured appendix. Her past history was entirely irrelevant. Her mother had been confined to a sanatorium for tuberculous patients for one year and had been discharged with a healed lesion at the apex of the right lung three years previously. The two lumps in the patient's neck had been present for six months. Two lower teeth on the right side had been extracted on the advice of a physician. The abdominal pain was characteristic of mild chronic appendicitis. The patient had lost about 5 pounds (2.3 Kg.) in weight during the past six months. The menstrual history was normal. There was no history of arthritis, fractures or pains in the joints.

Physical Examination—The tonsils had been removed in childhood. Examination of the eyes, ears, nose and throat otherwise gave negative results. The thyroid gland was palpable. Just below and to the right of the cricoid cartilage there was a spherical tumor 2.5 cm. in diameter, which appeared to be rather deeply seated in the neck but was freely movable and not attached to the skin. There was a somewhat smaller but tender mass in the submaxillary area. Examination of the chest gave negative results. There was abdominal tenderness at McBurney's point. Rectal examination revealed a small uterus. There was no adnexal tenderness. The ovaries were not palpable. Examination of the extremities gave entirely

12 Churchill, E. D., and Cope, O. Parathyroid Tumors Associated with Hyperparathyroidism, *Surg., Gynec. & Obst.* 58:255, 1934.

13 Cutler, M., and Owens, S. E. Irradiation of the Parathyroids in Osteitis Fibrosis Cystica, *Surg., Gynec. & Obst.* 59:81, 1934.

14 Albright, F., Aub, J. C., and Bauer, W. Hyperparathyroidism. A Common and Polymorphic Condition as Illustrated by Seventeen Proved Cases from One Clinic, *J. A. M. A.* 102:1276 (April 21) 1934.

negative results. Examination of the blood revealed the following values: hemoglobin, 90 per cent, erythrocytes, 4,400,000 per cubic millimeter and leukocytes, 7,500 per cubic millimeter, with polymorphonuclear neutrophils 62 per cent, lymphocytes 36 per cent and eosinophils 2 per cent. The coagulation time was three and one-half minutes. Urinalysis gave negative results.

Progress—The patient was admitted to the hospital on February 14. A diagnosis of mild chronic appendicitis and cervical lymphadenitis of undetermined type was made at the time of admission. Appendectomy was performed. The appendix was normal on gross examination. The abdomen was thoroughly explored, but no abnormality was found. A submaxillary lymph node measuring 15 mm in

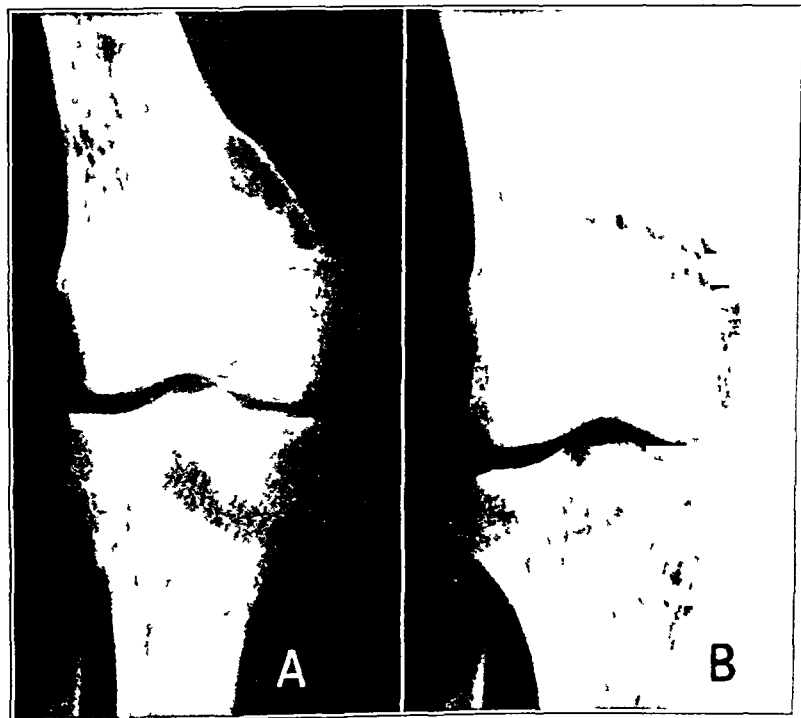


Fig. 3—Roentgenograms of the lower end of the right femur, *A* taken on Oct. 8, 1936, and *B* on Dec. 5, 1938. They show almost complete filling in of the cyst.

diameter was removed. The larger tumor in the neck was situated beneath the platysma muscle lying on the lower portion of the right lobe of the thyroid gland at its lateral border. This tumor was removed without difficulty. The postoperative convalescence was uneventful. The patient was discharged from the hospital on the sixth postoperative day.

Pathologic Report (O. A. B.)—The appendix was normal. The cervical lymph node exhibited chronic inflammatory hyperplasia. The remainder of the specimen consisted of an ovoid encapsulated mass measuring 23 mm in maximum diameter. It was rather soft and friable. On section it was homogeneous, opaque and

diffusely pink. Microscopic sections consisted entirely of an epithelial neoplasm which was apparently encapsulated. The individual neoplastic cells were columnar in early type and possessed clear or faintly staining cytoplasm. There was some irregularity in the size of the cells, some areas were composed of smaller cells which were somewhat basophilic. In the larger cell areas there was a definite arrangement into cords or tubules, with recognizable lumens in some instances. Throughout the tumor there was a rich vascular stroma, with conspicuous engorgement of blood vessels in some areas. The pathologic diagnosis was hyperfunctioning adenoma of a parathyroid gland.

Roentgen Report (Dr. R. W. McGloach)—There was considerable difficulty in persuading the patient to return for further observation, and roentgen examination was not made until May 2, two and one-half months after the operation. Roent-

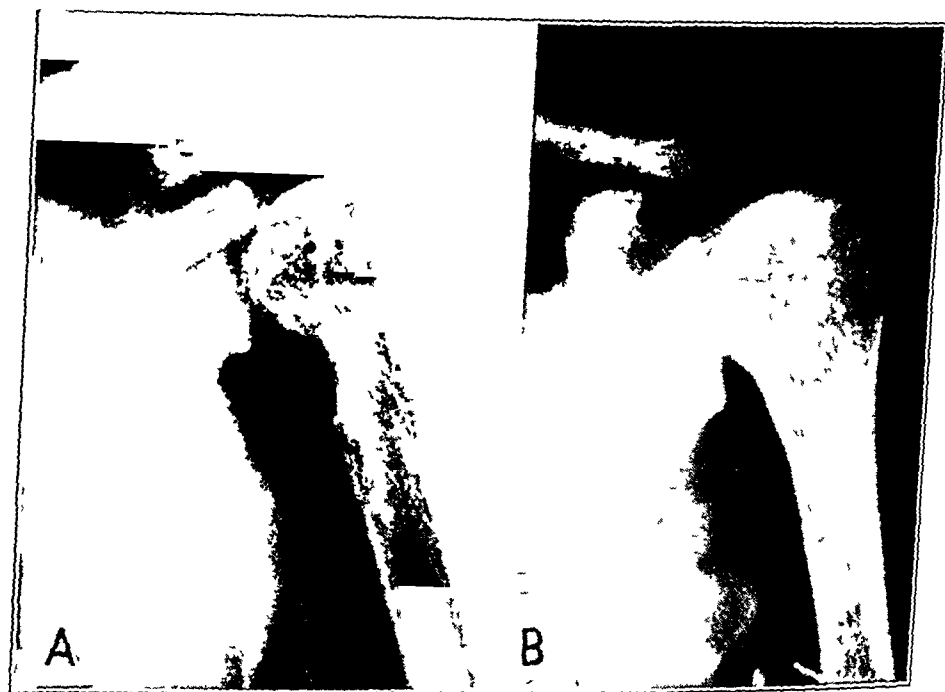


Fig. 4—Roentgenograms of the upper end of the left humerus, *A*, taken on Oct. 8, 1936, and *B* on Dec. 5, 1938.

genograms of the skull, hands, shoulders, knees and spine were taken. There was a fine granular mottling throughout all the bones, with marked irregularity and thinning of the trabeculae. The skull had a moth-eaten appearance, with small areas of increased density. There was a cyst in the distal extremity of the fifth metacarpal bone of the right hand, one at the upper end of the left humerus on the medial side just below the epiphysial line, one in the lower end of the right femur above the medial condyle and one at the upper end of the left tibia on the medial side. The roentgen diagnosis was osteitis fibrosa cystica.

Further Data—The first opportunity to examine the blood chemically was on May 2, two and one-half months after operation. At that time the calcium content of the blood was 10.5 Gm. per hundred cubic centimeters. The patient had no complaints, no disabilities and no symptoms referable to the extremities. Her posture was good. She received no further treatment. On October 8 she had no

complaints and physical examination gave negative results. She had gained 10 pounds (4.5 Kg) in weight in the past two years. Pain in the right lower quadrant of the abdomen had not recurred. On Dec 5, 1938, a check-up roentgen examination of the right hand, right knee and left shoulder revealed almost complete filling in of the cysts which were found in the distal end of the fifth metacarpal bone of the right hand, in the upper end of the left humerus and in the lower end of the right femur in the original examination. The trabeculations were still irregular and thickened and showed a tendency toward cyst formation. In a comparison of the roentgenograms with those taken on Oct 8, 1936, greater density in the trabeculations of the cyst was apparent.

COMMENT

The sequence of diagnostic and therapeutic events in this case was irregular, because the correct diagnosis was not suspected until the tumor had been removed and a pathologic report rendered. For this reason chemical examination of the blood was not made until too late to be of any value and roentgen examination of the skeletal system was delayed for the same reason. A clinical diagnosis of tuberculous cervical adenitis was made because (1) there were two masses in the neck and (2) there was a history of contact with tuberculosis. Pathologic examination revealed that the smaller lump in the neck was a hyperplastic lymph node. The cause of the hyperplasia was undetermined.

The unusual features of this case were as follows: 1. The patient was in the second decade of life in which only 6 per cent of parathyroid adenomas occur. 2. The tumor was palpable. 3. Excision was performed easily, in contrast to the difficulty frequently encountered in locating the tumor. 4. The adenoma apparently developed in an ectopic parathyroid gland. 5. The patient was cured of the primary disease before the correct diagnosis was suspected clinically.

The osseous lesions demonstrated roentgenographically had almost completely disappeared within eight months after the operation and the patient was entirely well in the interval. At the time of writing, after nearly three years, there is no clinical or roentgen evidence of recurrence. The symptoms leading to a clinical diagnosis of appendicitis were unexplained except that small renal calculi might have been present. Examination of the right kidney, however, did not reveal the presence of calculi.

SIMPLE STANDARD APPARATUS FOR TREATMENT OF COMPOUND FRACTURES OF THE HAND, FINGERS AND WRIST

REPORT OF A CASE AND EVALUATION OF
THE END RESULT

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The literature abounds with descriptions of all types of apparatus which have been of benefit in specific cases of fracture or severe injury of the hand and fingers. There is, however, no uniformly recognized method of making these appliances practical for all kinds of injuries to the hand and fingers. Moreover, I know of no appliance that can be said to be universally easy to procure when needed nor any that is as simple and safe to use as the one which is herein described.

The best therapy is often the most simple to prescribe and carry out for the really complicated compound hand injuries mentioned. The various principles of treatment of compound fractures of the hand and fingers need only to be mentioned in order to demonstrate the simplicity and ease of quick construction of my appliance.

The types of case in which the method applies are varied. It may be used for any or all of the following injuries:

- 1 Compound fracture of one or all fingers
- 2 Compound fracture of the hand and/or the thumb
- 3 Compound fracture of the wrist and/or fracture of the hand and/or fingers

The cost of materials for this apparatus is difficult to estimate, but it is negligible. The materials (fig 1) include the following:

- 1 Heavy wire-cutting pliers
- 2 Several steel wire coat hangers
- 3 Plaster of paris bandages (2, 3 and 4 inch [5, 7.5 and 10 cm] rolls, as used in standard hospitals)
- 4 Medium and small elastic bands (assorted), about one dozen
- 5 Round, straight cambric sewing needles (assorted sizes)
- 6 Adhesive tape

7 Six to twelve small corks

8 Heavy suture silk, such as is kept in a standard hospital operating room supply

9 Rolls of cotton batting and assorted gauze dressings and roll gauze bandages

10 Iron extension ring—a “banjo splint” or a substitute as described

The method of constructing the apparatus depends somewhat on the type and extent of the injury, as well as on the time after the injury when the patient is first seen

No digression from the individual surgeon's principles of treatment of compound fractures need be made. The apparatus is compatible

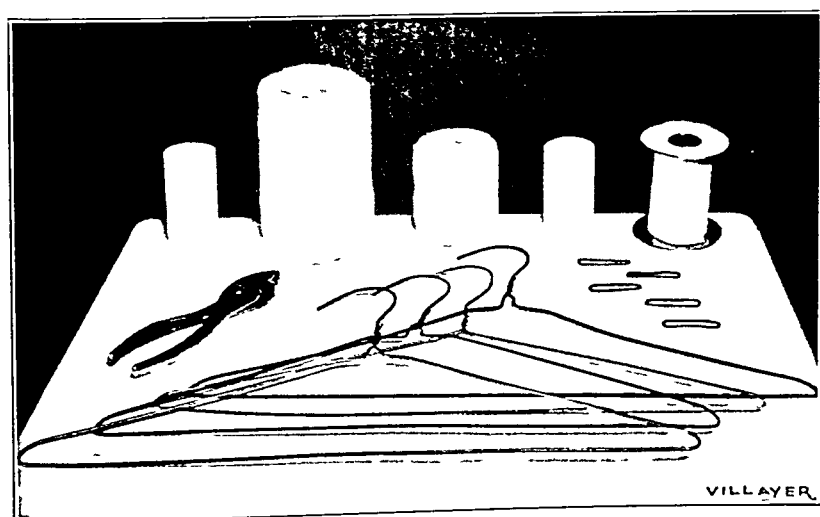


Fig 1—Essentials for construction of the apparatus: gauze rolls, padding, plaster of paris, adhesive tape, elastic bands, steel wire coat hangers and wire-cutting pliers. Sewing needles, corks and silk suture material are not shown.

with either “open” or “closed” treatment and may be adapted to either. It causes no shock in application, and in cases in which the patient is brought to the hospital in profound shock it may be put on without the slightest harm provided its limitations are understood. It will then be in position, so that the surgeon may later apply traction in any way he sees fit according to the roentgen indications.

Before entering on a description of the apparatus it is important to emphasize the main principles of the treatment of compound fractures. After these are in mind it will be seen that the method of treatment to be described complies exactly with these principles. Certain consideration must be given each case before any apparatus is con-

denied or accepted. The mechanism advocated in this communication, I believe, will withstand the most critical observation of specialists in the treatment of complicated fractures of the hand. The idea of the apparatus is probably not entirely original, the appliance is a combination of several kinds of apparatus, which have their own separate merits. One must learn how to use it after it is in place and must try it out to see its simplicity of action and its general practicability. It is certainly a reliable mechanism for making the treatment of severe injuries of the hand and fingers and even of the wrist a business-like and clear-cut standard procedure for every hospital.

The main principles in the treatment of all compound fractures can be briefly reviewed in a few words. First, the risk of infection must be minimized (regardless of the type of treatment used, whether "open" or "closed"). Second, satisfactory reduction must be aimed at even if it cannot always be achieved. Third, immobilization must be obtained and maintained at the direction of the surgeon and not be left to chance. Fourth, traction must be obtainable when necessary and if necessary must be uniformly maintained. Fifth, changes in the direction of traction must be possible with whatever apparatus is used, so that it may be possible to overcome a probably bad start in the treatment of the more severe and shocking accidental injuries. Sixth, early mobility should be possible. Seventh, the need of visibility and accessibility of the wounds of compound fractures can hardly be stressed too much when a mechanical aid is required, especially with injuries to the hand. Lastly, the patient's comfort must be considered from beginning to end if a good result is to be obtained. All these provisions can be carried out if the apparatus I describe is used wisely and modified to the needs of the individual patient.

One or two other suggestions about the treatment of compound fractures seem so obvious that they need only be mentioned to insure their not being forgotten or neglected. Shock and hemorrhage must at all times be the first considerations in the treatment of such injuries. One reason is that the hand and fingers have a large nerve supply, predisposing to more shock than is often supposed, and another is that the arteries of the hand and wrist are large and can be the cause of marked loss of blood, sometimes out of proportion to the visible injury.

One point to stress in the construction of a standard apparatus for fractures of the hand and finger with severely contused wounds is the proper application of one of the parts of the apparatus I shall describe. I refer to the plaster of paris portion of the mechanism. No plaster should be applied to any part of any extremity unless the part to be covered is clean and one is positive that no active or potentially dangerous infection is being covered.

Plaster, then in this apparatus must be thought of only as an agent to fix the extremity above the fractures, the wounds and the entire length of the broken bones (except those of the forearm in some cases) being left free and clear to be later immobilized by an entirely different means.

The plaster will serve only as a firm, safe foundation for other parts of the apparatus. The likelihood of applying plaster to an arm which may later become infected will be minimized if the plaster is not applied too tightly if the operator has had experience with its handling and makes sure that plenty of cotton batting is used before the plaster is rolled on.

When a hand is badly mangled up to the wrist I know of no better way of treating the injury than by this method, but provision must be made not to endanger the forearm from constriction below a safe point some inches above the wrist. The elbow should be flexed and

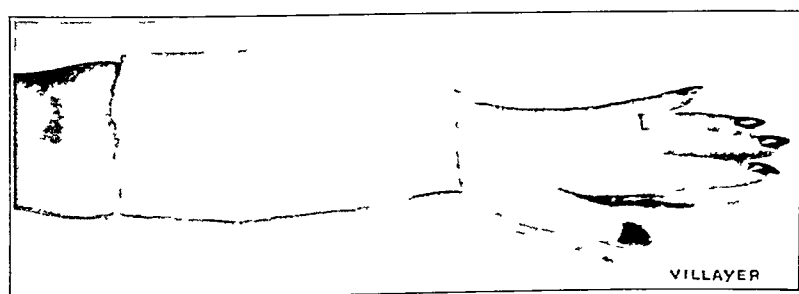


Fig 2—Application of plaster of paris between the wrist and the elbow, over ample padding, with sufficient plaster to make a firm foundation for the rest of the apparatus after this much has been allowed to harden.

the plaster cast carried halfway to the shoulder on the upper part of the arm in such a case.

Since a hint as to the procedure has been given the general structure of the apparatus may be discussed. Figure 2 illustrates the points where the plaster is first applied.

The plaster may ordinarily stop short of the elbow by a sufficient margin to insure comfortable flexion and should extend to the wrist where plenty of padding should be used before the plaster is put on.

This first application should be the thickness of a cast that will be solid but not bulky, usually requiring at least three to four rolls of 3 or 4 inch plaster. The plaster should be allowed to harden. Time will vary for this but it is most important that this foundation cast be firm, so that later applications of iron arms or the steel wire will not dent the plaster and possibly cut off the circulation or cause pressure necrosis.

The next step is to cut the flexible steel wire coat hangers so that plenty of straight pieces may be obtained. A straight length of at least a foot and a half (45 cm) when bent so as to form the general shape of a banjo head and handle will suffice to make the banjo splint extension ring that so often is hard to find when needed. If the wire from two more coat hangers is wrapped around this framework in the manner of a grapevine winding around a small branch of a tree, the banjo arm will be strong and inflexible. This assures a fixed radiating surface distal to the hand for the application of traction in the line of the forearm, as is shown in figure 3. If the iron banjo splint is available it may be utilized, of course, in place of the coat hanger wire.

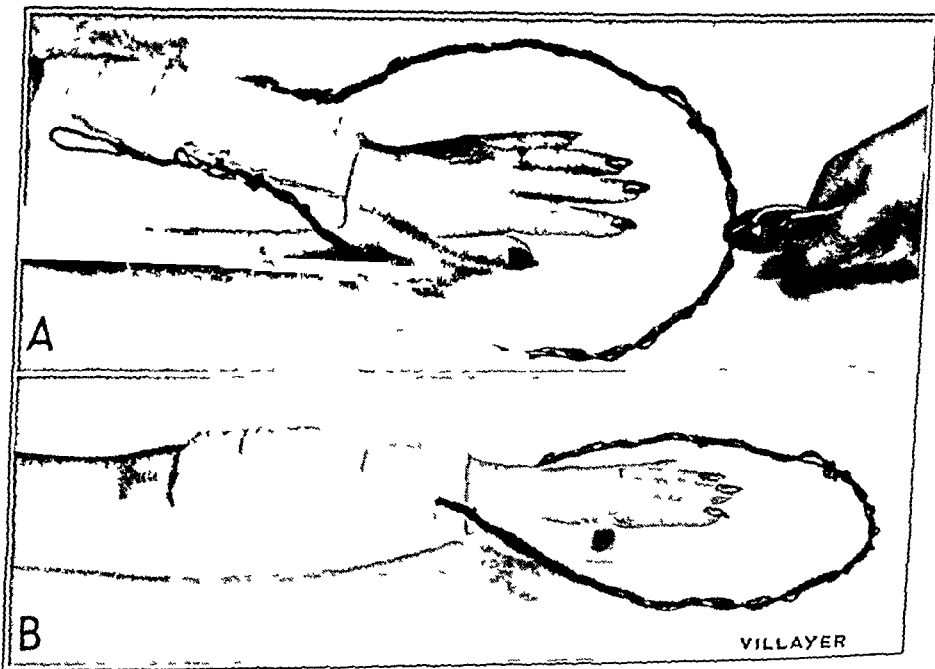


Fig 3—*A*, coat hanger wire bent in the shape of a banjo splint and reenforced by two more lengths of the same material, wound around it like a grapevine. This makes a strong "banjo splint" in a few moments. *B*, banjo splint incorporated into place by the addition of a few turns of wet plaster over the now solid foundation cast.

Next, it is important to decide just what kind of extension of the hand itself is needed and what amount of flexion of the hand and fingers seems indicated.

The procedure may be varied to suit the requirements of the given case. Two other modified "banjo arms" made of the coat hanger wire can be wrapped into the cast after fixation of the main banjo extension arm by one or two rolls of plaster. The shape of these two additional arms is illustrated in figure 4.

The apparatus is nearly finished and requires only the fixation which will be given by stabilization of the upper and lower wire arms. This is carried out by attaching their distal corners to measured lengths of the coat hanger wire (about 8 cm, with 1 cm ends bent at an angle of about 45 degrees), by means of a few turns of adhesive tape, as shown by figure 5. This completes the framework of the apparatus.

A clear description of the apparatus is difficult, but it is unbelievably simple to understand when it is tried on a patient.

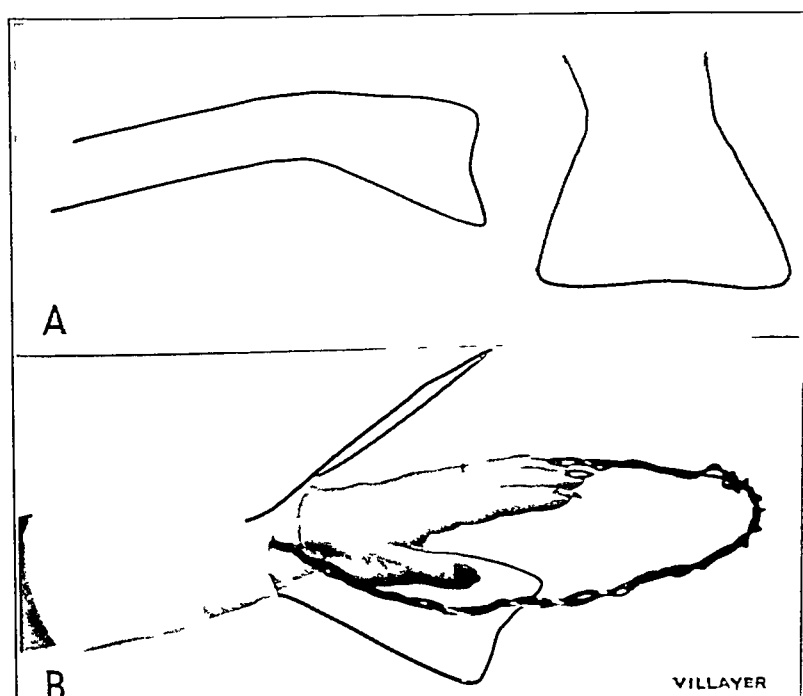


Fig 4—*A*, additional pieces of coat hanger wire bent into these shapes so as to furnish the two upper and lower modified "banjo arms." *B*, upper and lower "modified banjo arms" held in place by a few more turns of plaster over the foundation cast.

Shortening of the upper and lower arms is easy and is accomplished by the addition of cross wires fixed at right angles in the same way as the "fixation wires" by bending their ends followed by application of a few turns of adhesive tape.

An idea of the bare framework of the apparatus (without all the attachments to the fingers and countertraction attachments afforded by the use of muslin bandage around the fingers and extending over the side arms) is gained from simplified model photographs taken at a different angle (fig 6).

In a photograph the "upper" and "lower" arms of the steel coat hanger wire would be partly obscured by the turns of adhesive tape which hold the fixation wires in place and by the muslin bandage tied around the fingers so as to provide countertraction when necessary, in the direction of either the "upper" or the "lower" cross arm, therefore, no attachments of any sort are shown in the model pictures. The small snapshots in figure 7 show the actual apparatus as used in the case herein reported.

Little further explanation is necessary to illustrate how easily the wounds on the dorsal or palmar side (or both) of the hand and fingers

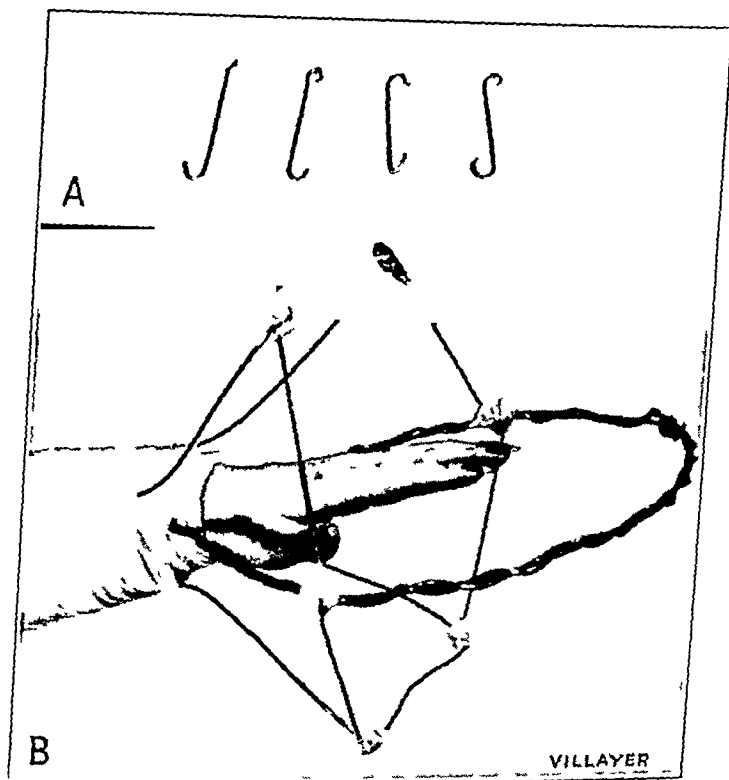


Fig 5—*A*, lengths of coat hanger wire, about 8 cm long with 1 cm ends bent at an angle of 45 degrees, make satisfactory side arms with which to stabilize the upper and lower "modified banjo arms" by attaching them to the main banjo splint. *B*, bare framework of the apparatus completed by attachment of the 8 cm lengths of wire from the upper and lower arms to the main banjo splint by adhesive tape. It is easy now to see how attachments can be utilized for extension and counterextension in almost any direction.

can be reached or to show how extension and countertraction in all directions can be obtained by using rubber bands, attaching them by an interposed silk suture either to a finger nail or to the ends of a needle inserted through the fleshy tip of the finger, as shown in figure 8 or by adding extra cross wires to change the line of pull (not shown).

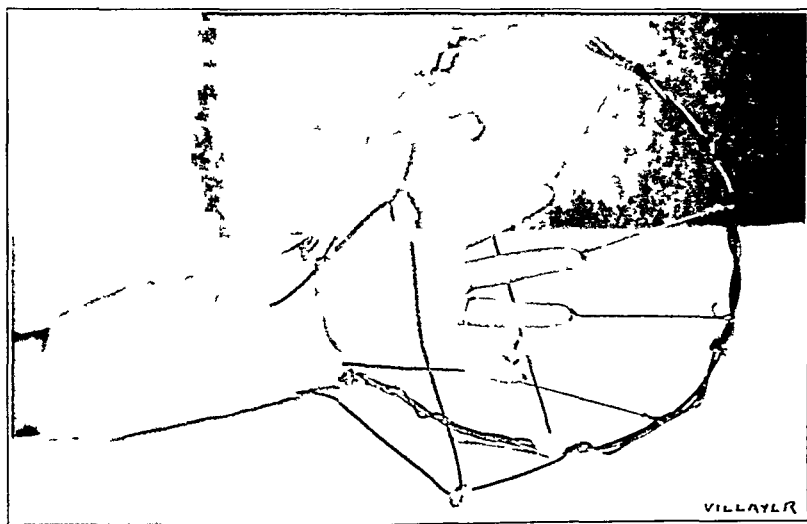


Fig 6—Bare framework of the apparatus in another view with elastic bands connecting the model's finger nails to the main banjo splint. Actually the finger nails may be used for extension by threading them with silk suture material and attaching the silk to the elastic and, in turn, the elastic to the banjo splint. Counter-extensions by bandages connected with the upper and lower arms are not illustrated in this photograph, but may be seen in figure 7.

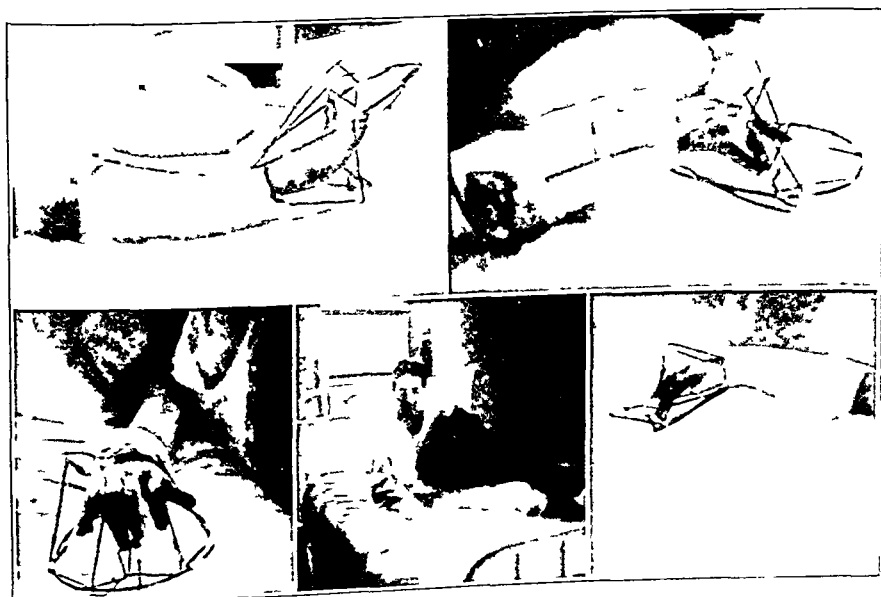


Fig 7—Views of the patient whose case is here reported illustrating the mobility of the hand and the counterextension utilized on the ring finger by a muslin sling connected to the upper arm of the apparatus. The details of extension for the fingers are difficult to see, but the hand and fingers are held in a balanced traction by elastic bands attached to the ends of the fingers (either by a silk suture through the finger nail or by a needle threaded into the tip of the finger as shown in figure 8).

Another type of cross arm, well padded and carefully bent into place, may be applied to the base or dorsum of the wrist, as shown in figures 9 and 10, if the cast cannot be applied as far distally as the wrist because of lacerations or fractures near the bases of the metacarpal bones

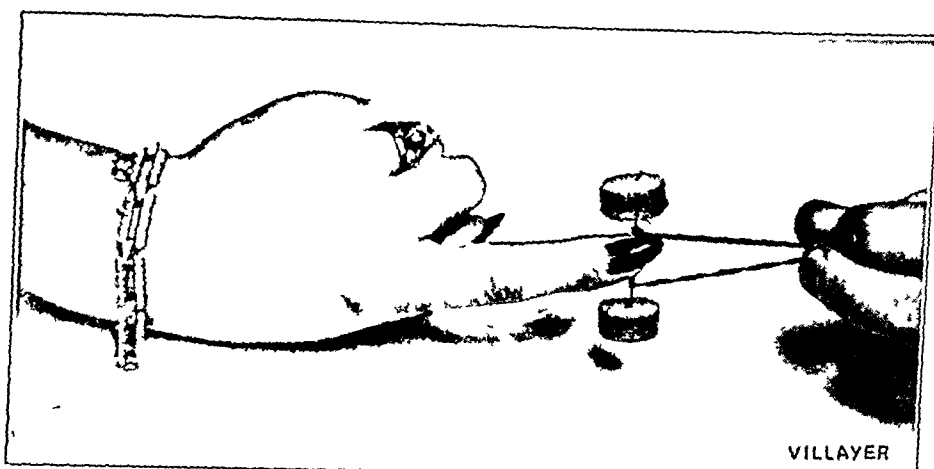


Fig 8—Method of attaching the elastic rubber band to the needle which is inserted through the fleshy tip of the finger. Protection of other fingers is provided by corks covering the ends of the needle

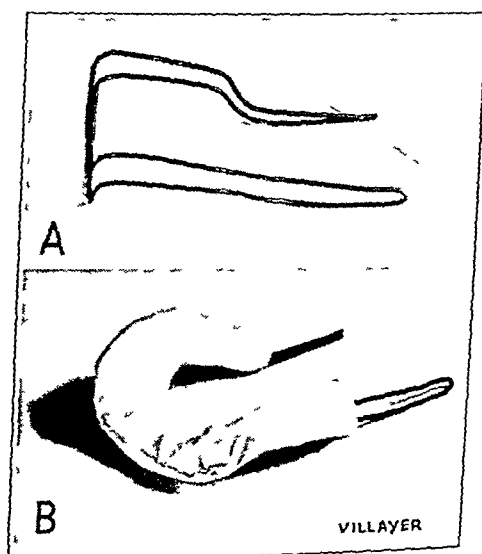


Fig 9—A, another piece of coat hanger wire, properly bent as shown. This makes an ideal support which can be added to the foundation cast if because of extensive lacerations on the flexor side of the wrist the foundation cast cannot extend far enough distally to support the wrist. B, same, padded and wrapped with gauze

It is seen, then, that the method depends on the needs of the patient and on the physician's understanding of what is required for the treatment of all the different kinds of fractures of the hand and finger. Briefly, there is no other way than to study the needs of each case.

fracture, as to displacement, applicability of extension, applicability of counterextension and general applicability of the apparatus

In the case here reported, for example, all the fingers of the right hand were involved, and it was found that one of the compound fractures of the ring finger was not satisfactorily reduced by comparatively straight extension during the first few days. It was simple to change the direction of pull after a day or two so that the finger was flexed at the joint between the first and second phalanges and pull in two directions exerted so as to overcome the likelihood of further

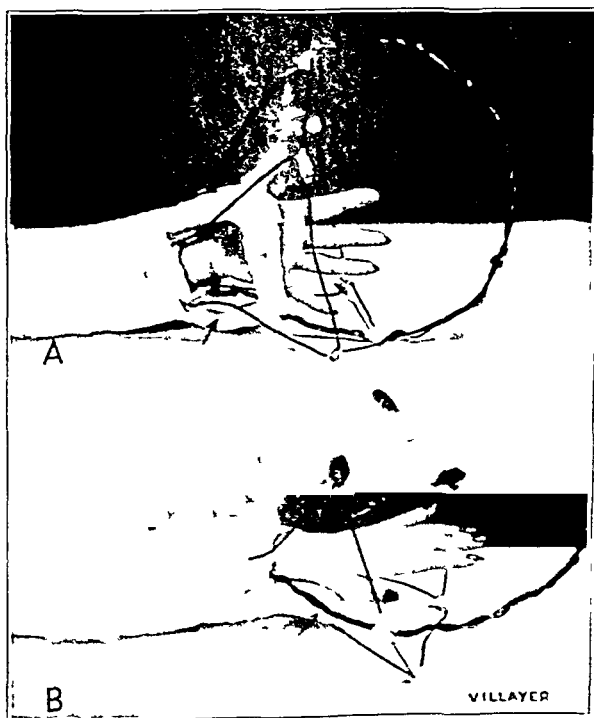


Fig 10—*A* same general apparatus. The supporting arm shown in figure 9 is in place and is indicated by the arrow. *B* different view showing the supporting arm (indicated by the arrow) well padded and incorporated under the hand. A few more turns of plaster have been wrapped around it and around the foundation cast above the wrist.

displacement and to provide better reduction of the fracture of the middle phalanx.

The wounds on the dorsum of all the fingers as well as those on the palmar side, were simple to dress but the dressing would have been difficult if any other kind of splint had been used to rest the fingers on or if the splint had had to be moved only.

The case to be reported illustrates the simplicity and advantage of treatment with this apparatus. A detailed description of the injuries and final photographs of the hand six months after the injury, showing about 85 per cent return of function (about 75 per cent if considered cosmetically alone) are given. There was no complicating infection.

REPORT OF CASE

L. C., a man aged 20, a feeder on a dye cutter, was first seen at the New York Post-Graduate Medical School and Hospital on May 27, 1937, about twenty minutes after having caught all the fingers of the right hand in a dye cutter. He described the injury as a crushing one, but added that the cutter allowed about 1 cm. of clearance at most, so that part of the injury was due to his instinctive attempt to extricate his hand as it was being mashed.

General physical examination gave essentially negative results except for a fairly rapid pulse rate (about 100) and some degree of shock, there were pallor, weakness, sweating and nervousness. The urine was normal.

Both hands showed considerable discoloration with printer's ink. All the fingers of the right hand were blood stained, and had obviously undergone a severe crushing injury. It was difficult to tell which fingers were most injured. The middle finger was bleeding the least and appeared almost necrotic at first sight. The patient was not closely examined further but was admitted to the hospital after roentgen examination and was sent to the main operating room. No further treatment or examination was done preoperatively. A loose sterile gauze bandage was applied to the hand.

Operation (with the patient under nitrous oxide-ether anesthesia) consisted in careful sterilization of the hand and forearm with tincture of iodine and débridement of the edges of skin along some of the lacerations. Sterile saline solution was used to wash the depths of the wounds. Purified petroleum benzine, alcohol, saline solution and a repetition of the application of iodine were used where grease and dirt were adherent. A small bit of adhesive tape was removed from one of the fingers where the patient had had a small cut a few days before the present injury.

Examination was done in the operating room *at this time*, and not before. The roentgenograms were now available, and the patient was not subjected to any traumatizing handling of the fingers further than that needed to clean the wounds and make sure that no important ligaments or tendons were neglected.

Many lacerations were present, best portrayed by the shaded areas shown on the photographs in figure 11.

Roentgenograms demonstrated comminuted fractures of the midphalanges of the index, middle and ring fingers. There was avulsion of the extensor tendon of the middle finger at the first interphalangeal joint. The corresponding joint of the index finger and the distal joint of the extensor side of the little finger showed compound fractures, were lacerated and lying open. There were dislocation of the terminal phalanx and an avulsion of the nail of the little finger, which also showed a compound fracture.

It should be repeated that no blood was encountered on exploration of the badly injured middle finger. Hemostasis was obtained in all the other fingers and all the wounds were partly closed with a total of only about five or six fine silk sutures. No flexor tendons were lacerated, although all were exposed on the palmar side in all the fingers. The tears in the capsules of the joint were

repaired, nor was the inch or so of extensor tendon of the middle finger replaced. Instead it was cut off cleanly, because of its devitalized appearance.

Silk suture material was inserted through the nails of the index and middle fingers. Cambric sewing needles were used through the fleshy part of the ring and little fingers. The ends of the needles were covered by corks (fig 8).

Next an apparatus consisting of the cast previously described and a cast iron "banjo extension ring" splint was used. A similar mechanism has been illustrated in the photographs. Figure 7 shows the one actually used.

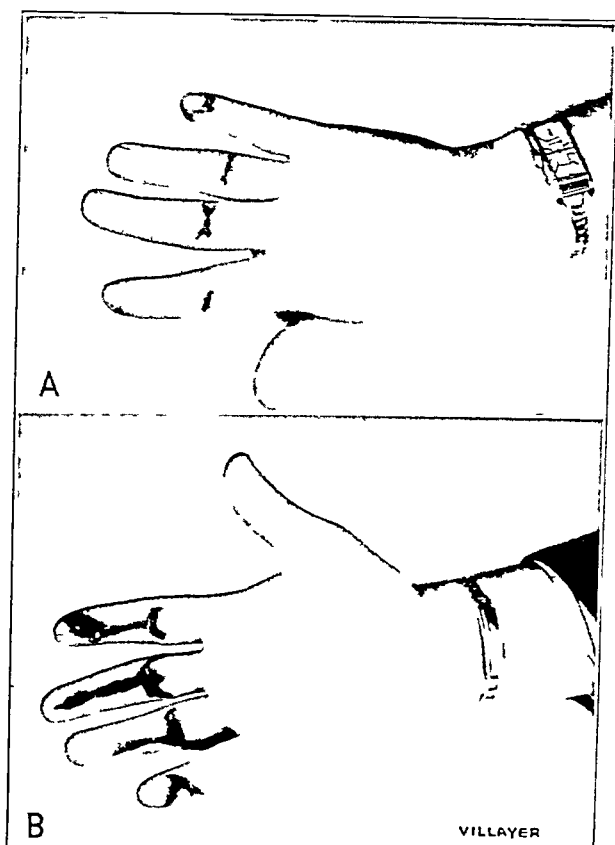


Fig 11—*A*, print of the left hand reversed, so that it appears to be the right hand. The shaded areas illustrate the lacerations on the dorsal side of the fingers where compounded joint lacerations and compound fractures coexisted. Compare with the final result eight months after injury (figs 13, 14 and 15). *B*, areas of laceration and cutaneous involvement over the exposed joints, fractures and deep tendons on the flexor side. Compare with the final result eight months after the accident, shown in figures 13, 14 and 15.

The fingers were moved little or not at all to minimize trauma and extension was held lightly by the silk sutures to the iron ring distally. No attempt was made to exert elastic tension on the fingers at this time because of the severity of the injuries and the danger of further loss of circulation with the onset of post-operative edema and congestion.

On the next day, when it became certain that circulation would continue satisfactorily and that amputation of any of the fingers would probably not be required, the apparatus was augmented by elastic band extension on the fingers.

Postoperative roentgen examination was thought less important for a few days than care of the wounds. No method of splinting the fingers could have been more satisfactory than the method used.

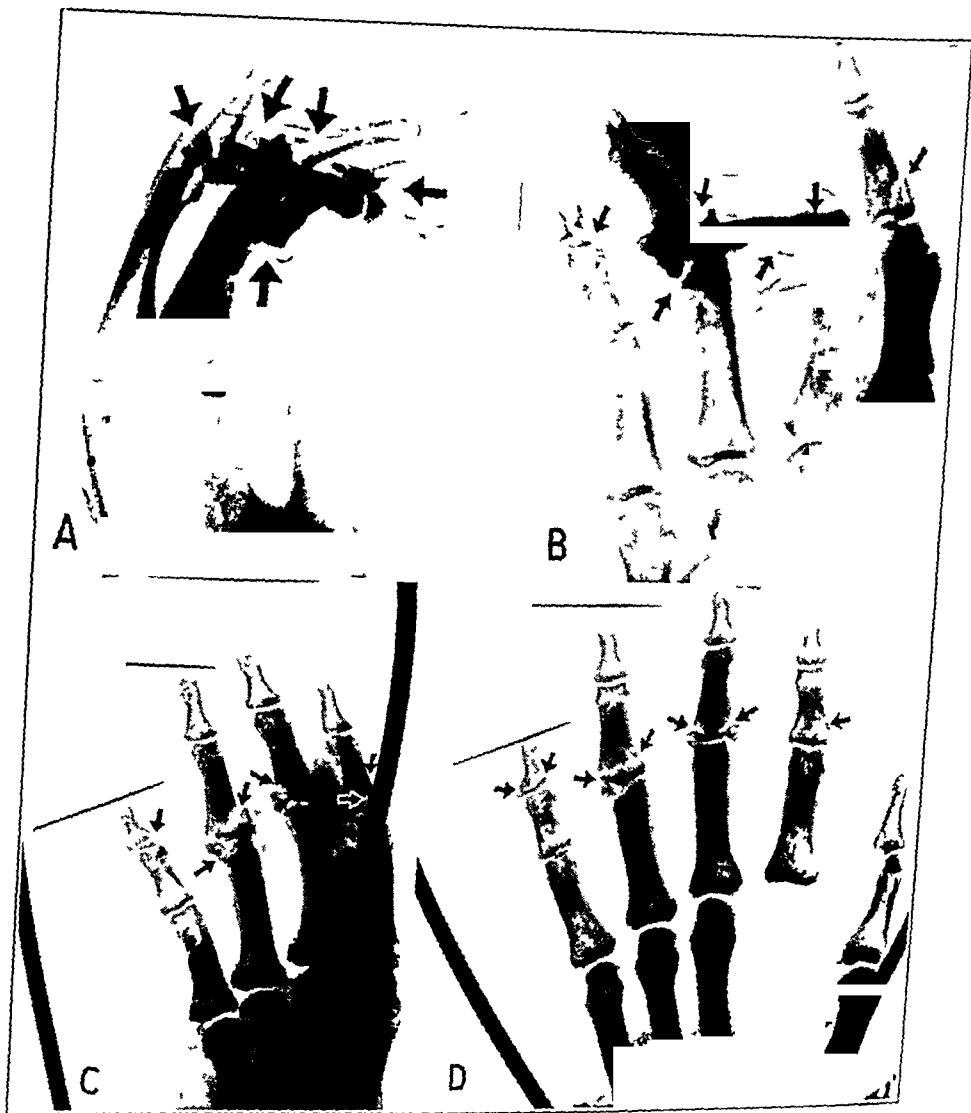


Fig. 12—*A*, oblique fracture on the external side of the base of the middle phalanx of the index finger. There is much capsular and soft tissue swelling. *B*, comminuted fracture of the base of the middle phalanx of the middle finger, with a vertical fissure involving the articular surface. Swelling of the capsule and of the soft tissues is present. *C*, comminuted fracture of the middle phalanx of the ring finger, with a vertical fissure line involving the articular surface, fracture at the mesial border of the head of the proximal phalanx, and slight palmar displacement of the major distal fragment of the middle phalanx. There is considerable capsular and soft tissue swelling. *D*, comminuted fracture at the base of the terminal phalanx of the little finger, partly intra-articular, with capsular and soft tissue swelling.

When healing seemed to have begun, roentgenograms were taken and all the fractures except that of the ring finger seemed to be fairly well reduced. It was at this time (about the fifth day) that the additional wire 'arms' were added to the cast and braced with the stabilizing "fixation" wires of the same material, so that the apparatus could be utilized in a different way for one of the fingers, the ring finger. The application of a muslin bandage around the proximal phalanx of the ring finger and a change in the pull of the rubber extension band provided the difference in therapy indicated by the roentgenogram. Further displacement of the proximal fragment of the middle phalanx anteriorly was thus prevented,

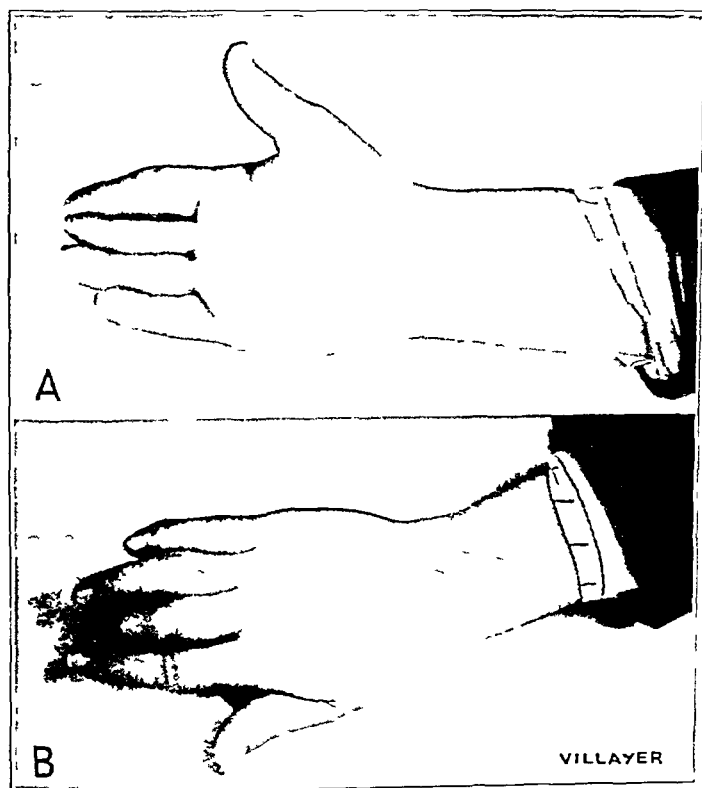


Fig 13—*A*, result eight months after the accident. *B* same viewed from the dorsal side.

and the chance of better reducing the distal fragment of the middle phalanx was increased. The mechanism succeeded fairly well and could have been easily modified again had it been found necessary.

By the third postoperative day the patient was encouraged to move the fingers slightly and not to mind the dressings, which consisted of careful removal of crusted blood and serum. At the time of the dressings the fingers were gently massaged toward the hand by means of small peroxide sponges. The patient volunteered the statement that the hand always felt better after the dressings. He had no pain and required sedatives only for a night or two.

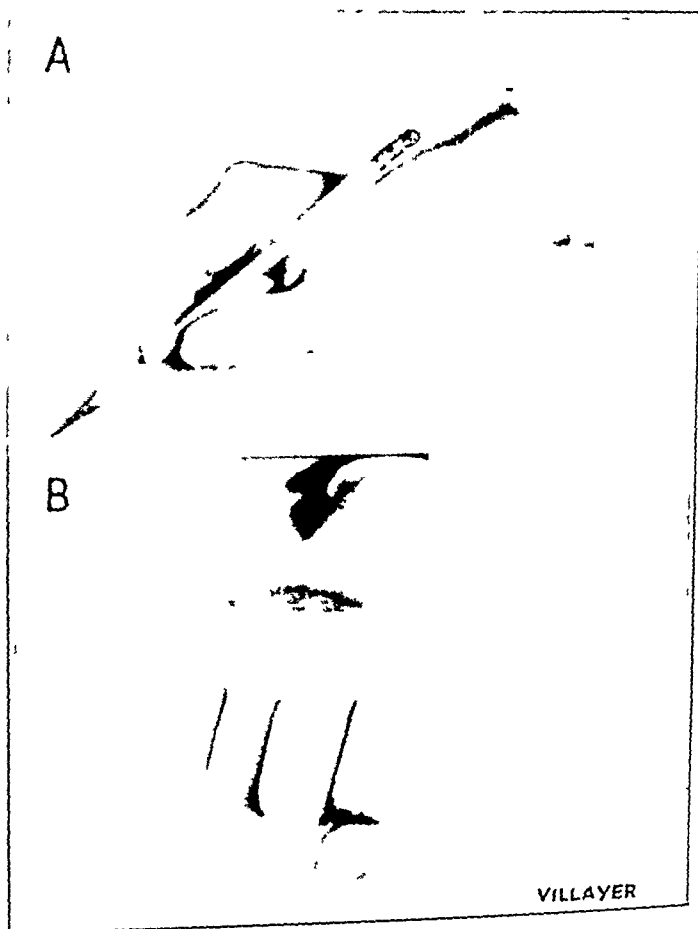


Fig 14—A, final result viewed from the side as the patient writes B, final result showing a view of the fist the patient can make

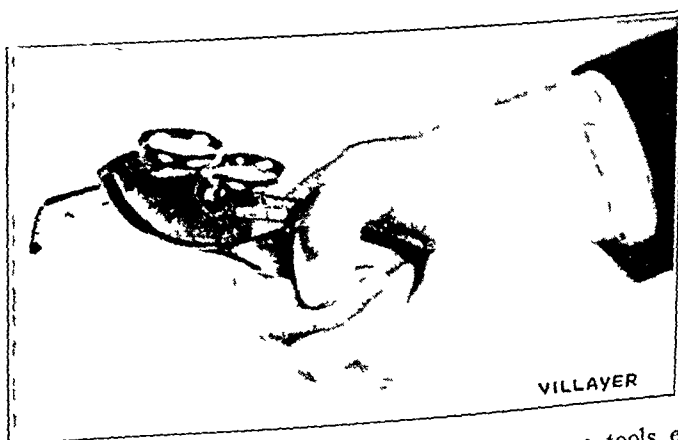


Fig 15—Final result showing the patient's ability to use tools eight months after the accident

Shock played a part in this case in that the patient could eat little and drink less for the first three days after the operation. Dextrose in saline solution was given intravenously on two occasions to counteract the gastric disturbances and compensate for the patient's inability to take in enough by mouth to offset the postoperative reaction and dehydration.

No infection occurred, partly owing to the use of strict aseptic technic from beginning to end. The wounds remained healed except for slight necrosis at the tip of the middle finger, at the base of the nail for about two weeks. Culture of the exudate was sterile at the end of seventy-two hours.

The fingers were released from the apparatus at the end of four weeks, and the patient was instructed in detail about exercises and baths thereafter. Baking and massage were instituted in his daily regimen.

What the patient required more than anything else was repeated encouragement and example as to the type of exercise and the means of increasing the usefulness of the hand. It was difficult to convince him of the need of continuous effort over a period of months.

About nine weeks after the accident there was approximately 70 per cent return of function. At the time of writing the cosmetic result is better than fair. There is some loss of soft tissue at the tip of the middle finger. There is inability to extend the middle finger completely at the distal two joints. The joints between the proximal and middle phalanges of the index, middle and ring fingers, all of which were badly lacerated, have remained somewhat larger in circumference than normal. The terminal joint of the little finger healed, and a new nail appeared, fortunately without any deformity to speak of.

The end result is illustrated by photographs taken eight months after the accident (figs 13, 14 and 15).

[NOTE—On April 20 1939, nearly two years after the operation, the patient appeared to have suffered no retrogressive changes and had not the least complaint the functional end result having remained the same as was observed seven months after the operation.]

SUMMARY AND CONCLUSIONS

Much has been written about special mechanisms and apparatus of all kinds for treatment of fractures of the hand and fingers but little about simplification of the treatment of compound fractures in the same location, although this is a problem of vast importance to industrial surgeons and surgeons dealing with traumatic conditions, as well as to practitioners everywhere.

A definitely inexpensive efficient and easy means of treating such injuries, particularly the worst lacerations and compound fractures with especial regard to apparatus, is described in sufficient detail to recommend consideration of its adoption in almost all cases under nearly all hospital conditions. The materials required can be found in even the less expensively equipped institutions at a moment's notice.

A short review of the rules of treatment of compound fractures is included. The most important considerations in the treatment of compound fractures of the fingers and the hand are listed.

The case of a patient who suffered a mangling injury of all four fingers of the right hand, with several compound fractures, compound joint luxations, avulsion of a tendon and lacerations of both sides of the finger is described in detail up to eight months after the injury. The case illustrates the ease and efficacy of the management of such a severe injury with this apparatus. The estimated percentage of return of function is higher than might be expected from the use of other splints or mechanical aids.

There is a real need of better recognition of the importance of severe injuries of the hand and fingers and the best basic means of treating them. I believe I have shown a method which is possible, safe, efficient, inexpensive and uniform. It may be employed under different conditions and in various localities and is available to all physicians everywhere.

525 Park Avenue

CALCIFICATION OF THE SUPRASPINATUS TENDON

CAUSE, PATHOLOGIC PICTURE AND RELATION TO THE
SCALENUS ANTICUS SYNDROME

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A pathologic condition of the shoulder with a calcareous deposit which casts a shadow roentgenographically has become an increasingly popular subject since it was first described by Painter¹ in 1907. Nevertheless failure to correlate the cause, the pathologic picture and the pathogenesis with the symptoms seems to be rather general.

This article is an attempt to correlate the pathologic lesion with the symptoms produced and to rationalize the treatment.

INCIDENCE

Calcareous deposits about the shoulder are much more common than is generally believed. In reporting 200 cases of "periarthritis of the shoulder" Dickson² found that 33.3 per cent showed a calcified deposit as revealed by the roentgenogram. Carnett,^{3a} by routinely taking roentgenograms of both shoulders disclosed that one fourth of his patients had bilateral deposits, only one shoulder being symptomatic at the time of examination.

Since the adoption about one year ago of a new routine for roentgen examination of the shoulder a diagnosis of calcification of the supraspinatus tendon has been made in a series of 27 patients, 9 of whom had bilateral deposits. One additional patient had a calcareous deposit in the subscapularis tendon.

The occurrence of such deposits is uncommon before the thirtieth or after the fiftieth year of life. The youngest patient in my series

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1 Painter, C. F. Subdeltoid Bursitis, *Boston M & S J* **156** 345-349 1907.

2 Dickson, J. A., and Crosby, E. H. Periarthritis of the Shoulder. An Analysis of Two Hundred Cases. *I. A. M. A* **99** 2252-2257 (Dec. 31) 1932.

3 (a) Carnett, I. B. The Calcareous Deposits of So-Called Calcifying Subacromial Bursitis, *Surg. Gynec. & Obst.* **41** 404-421 1925. So-Called Subacromial Bursitis, *S. Clin. North America* **10** 1309-1317 1930. So-Called Calcifying Subacromial Bursitis, *Radiology* **17** 505-513 1931. (b) Carnett, I. B. and Case, E. A. A Clinical and Pathological Discussion of So-Called Subacromial Bursitis, *S. Clin. North America* **9** 1107-1126 1929.

was 51 and the oldest 68. Men usually are affected more often than women (2 to 1), but in the 28 recent cases 18 of the patients were female.

ANATOMY

Codman⁴ in 1906 published the first adequate description of the subacromial bursa. He has since emphasized its mechanical importance and its relation to pathologic changes in the supraspinatus tendon.

The capsule of the shoulder joint in its superior portion blends with and becomes indistinguishable from the conjoined tendon of the short rotators as they course to their insertion into the tuberosities of the humerus. The tendon of the supraspinatus muscle reinforces the central portion of the capsule and is inserted into the anterior and uppermost part of the greater tuberosity. This attachment is just posterior to the bicipital groove, which may be palpated 2 fingerbreadths lateral to a line drawn vertically upward from the center of the cubital fossa when the elbow is flexed to a right angle.

The thin synovial lining of the subacromial bursa is tightly adherent to the tuberosities of the humerus and to the adjacent part of the conjoined tendons near their insertion to form its base and to the under surface of the acromion and adjacent structures to form its roof. On the whole, the bursa is circular, concavoconvex and somewhat smaller than the palm of the patient's hand, extending below the edge of the acromion as much as $1\frac{1}{2}$ inches (3.7 cm.) at its lowest point. It is separated from the shoulder joint only by the conjoined tendons of the short rotators.

ETIOLOGY

Concerning the cause of calcareous deposits about the shoulder, it is fairly well agreed that the sequence of changes leading up to the deposition of calcium is primarily interference with the blood supply. There is considerable controversy, however, as to how these changes are brought about. Codman and Wright, some time after the publication

4 Codman, F. A. On Stiff and Painful Shoulders. The Anatomy of the Subdeltoid or Subacromial Bursa and Its Clinical Importance, *Subdeltoid Bursitis*, Boston M. & S. J. **154** 613-620, 1906, *Subacromial Bursitis, or Peri-Arthritis of the Shoulder Joint*, *ibid* **159** 533-537, 576-582 and 756-759, 1908, On Stiff and Painful Shoulders as Explaining Subacromial Bursitis and Partial Rupture of the Supraspinatus, *ibid* **165** 115-120, 1911, Abduction of the Shoulder. An Interesting Observation in Connection with Subacromial Bursitis and Rupture of the Tendon of the Supraspinatus, *ibid* **166** 890-891, 1912, Obscure Lesions of the Shoulder. Rupture of the Supraspinatus Tendon, *ibid* **196** 381-387, 1927, Rupture of the Supraspinatus Tendon, *Surg., Gynec. & Obst.* **52** 578-586, 1931, The Shoulder. Rupture of the Supraspinatus Tendon and Other Lesions In or About the Subacromial Bursa, Boston, Thomas Todd Company, 1934. Codman, E. A., and Akerson, I. B. The Pathology Associated with Rupture of the Supraspinatus Tendon, *Ann. Surg.* **93** 348-359, 1931.

of the first reports of rupture of the supraspinatus tendon, advanced the hypothesis that calcium is laid down in the unabsorbed hemorrhage which fills the defect in an abortive attempt at repair of minor injuries to the tendon tissue which normally has a poor blood supply. Moschocowitz⁵ and Elmslie⁶ arrived at a similar conclusion. Carnett³ recorded his opinion that the deposits are, as a rule, quiescent in their formation and are due to tendinitis local necrosis of the tendon and calcification produced by often repeated occupational traumas which squeeze the supraspinatus tendon between the tuberosity of the humerus and the root of the subacromial bursa. Brickner advanced the hypothesis of a metabolic factor, but his theory was not convincing.

In discussing pathologic calcification in general, Wells⁷ concluded as follows:

Any area of dead tissue that is not infected, and that is so large or so situated that it cannot be absorbed, probably will become infiltrated with lime salts. Most frequently calcified, next to totally necrotic tissues, are masses of scar tissue that have become hyaline subsequent to the shutting off of circulation in the scar by contraction of the tissue about the vessels. The calcium salts come from the blood where they are held in solution or in suspension by the proteins of the plasma in an unstable condition capable of being overthrown by the increased alkalinity of the blood resulting from changes in the carbon dioxide content. In the areas that are to become calcified, the circulation is very feeble, the blood plasma seeping through the tissues as through any dead or foreign substance of similar structure without the presence of red corpuscles to permit of oxidative changes and the consequent production of carbon dioxide. The increased alkalinity resulting from the low carbon dioxide content of the tissue fluids renders the inorganic calcium carbonate and phosphate solution unstable and accounts for the gradual deposition of these salts.

Codman,⁴ Wilson,⁸ Fowler⁹ and others have operated on shoulders and found complete rupture of the supraspinatus tendon following such minor traumas as sudden elevation of the arm to regain balance when a person is about to fall. It seems reasonable to assume that if such minor traumas will produce a tear through the entire thickness of the tendon, it should not be an uncommon occurrence for a few fibers to be torn in the center or for an incomplete rupture to occur with few or minor symptoms. Such a lesion would heal as any wound does and on

5 Moschocowitz E. Histopathology of Calcification of the Supraspinatus Tendon as Associated with Subacromial Bursitis. *Am J M Sc* **150** 115-126 1915

6 Elmslie R C. Calcareous Deposits in Supraspinatus Tendon. *Brit J Surg* **20** 190-196 1932

7 Wells H G. Chemical Pathology, ed 5 Philadelphia W B Saunders Company 1925 pp 489-496

8 Wilson P D. Complete Rupture of the Supraspinatus Tendon. *J A M A* **96** 433-439 (Feb 7) 1931

9 Fowler E B. Stiff Painful Shoulders Exclusive of Tuberculosis and Other Infections. *J A M A* **101** 2106-2109 (Dec 30) 1933

frequent repetition of the injury would lead to areas of hyaline degeneration. Most patients who have painful calcareous deposits cannot recall having had an injury sufficient to be disabling or even inconvenient and may well have had such a sequence of events. It seems likely, then, that deposits in the tendons about the shoulder are laid down slowly in the areas of hyaline degeneration subsequent to repair of repeated minor injuries.

In favor of this hypothesis and in accord with my findings, Carnett and Case^{7b} and Moschocowitz⁸ working independently, recorded as a negative finding the absence of blood pigment in any of the many sections they examined. As seen in the roentgenograms and as reported at the time of surgical removal or at autopsy,⁹ the location of the deposit is usually in the tendon of the supraspinatus muscle near its insertion into the greater tuberosity of the humerus—the site in which rupture occurs most frequently (fig. 1). This part of the tendon lies in the groove between the tuberosities and the rounded head of the humerus and is, therefore, not the part to receive the greatest damage when squeezed between the bone and the roof of the subacromial bursa, as has been stated by those favoring the occupational theory. Also, in a series of 340 shoulders examined at autopsy, Fowler⁹ described more than one third (17 of 44) of the patients with rupture of the supraspinatus tendon as having a calcareous deposit in the area of attempted healing about the defect.

One should not be misled by the term "tendinitis" as it was used by Moschocowitz⁸ in rendering the first account of the histologic changes of this condition. From his descriptions of the microscopic picture it is clear that what he had in mind was mechanical inflammation and reaction to the foreign body rather than reaction to an infectious agent. One should recall, when considering the possibility of an infectious factor, that all cultures reported have been sterile. The presence of infection with the associated infiltration of inflammatory cells would increase the local metabolism and, consequently, the carbon dioxide content of the area. This would lead to an unsaturated condition of the tissue fluids—a chemical imbalance which accounts for the absorption of deposits of long standing subsequent to the reaction accompanying an acute flare-up.

A similar condition is encountered occasionally in calcification of the achilles tendon following trauma or surgical lengthening. Likewise, rider's thigh and calcification of the ligaments about the knee are conceded generally to be consequent to trauma.

9a. Keves, E. L. Anatomical Observations on Rupture of Supraspinatus Tendon, *Ann. Surg.* **97**: 849-856, 1933. Keyes, E. L. Anatomical Observations on Senile Changes in the Shoulder, *J. Bone & Joint Surg.* **17**: 953-960, 1935. Skinner, H. A. Anatomical Considerations Relative to Rupture of the Supraspinatus Tendon *ibid.* **19**: 137-151, 1937.

PATHOLOGIC PICTURE

Painter¹ rendered the first report of a case of calcareous deposit about the shoulder in 1907 but was in error as to both location and composition of the deposit, thinking it to be due to thickening of the walls of the bursa. Also it has been suggested that this shadow-casting substance was due to the accumulation of scar tissue (Baer¹⁰), to fluid under pressure, a hemorrhage (Beltz¹¹) and to metamorphosed fat deposits (Stern¹²). It is assumed that these investigators searched only in the bursa for the pathologic material, though Codman in 1908, reported the surgical removal of deposits composed chiefly of calcium from beneath the bursa in or on the supraspinatus tendon. This finding



Fig 1—Roentgenogram showing the usual site of calcified areas in the supraspinatus tendon. The mass was completely surrounded by tendon tissue and produced an elevation of the base of the subacromial bursa but showed no signs of local inflammation.

was soon confirmed by Wrede¹³ later by Brickner¹⁴ and still later by others. These authors found the deposit to contain calcium and to

10 Baer W S. The Operative Treatment of Subdeltoid Bursitis. *Bull Johns Hopkins Hosp* **18** 282-284 1907.

11 Beltz, cited by Berry J W. *Am J Orthop Surg* **14** 476-483 1916.

12 Stern W G. Metamorphosed Fat Deposits in Subdeltoid Bursitis. *Surg Gynec & Obst* **40** 92-94 1925.

13 Wrede L. Ueber Kalkablagerungen in der Umgebung des Schultergelenks und ihre Beziehungen zur Periarthritis scapulo-humeralis. *Arch i klin Chir* **99** 259-279 1912.

be located beneath the base of the bursa, usually in relation to the tendon of the supraspinatus muscle but occasionally associated with the subscapularis and less frequently with the infraspinatus tendons

The amorphous calcium phosphate and oxalate form a mass between the hyaline connective tissue fibers which fill the defect in the tendon (fig 3), having no capsule or limiting membrane and being surrounded by an area of local degeneration usually the width of only a few fibers. Such calcareous deposits are supposedly never primary in the bursa (fig 2) but lie beneath its base, in or on one of the tendons of the short rotators (fig 4). They vary greatly in consistency, being soft



Fig 2—Extensive calcification of the supraspinatus tendon, which appears in the roentgenogram to be within the bursa. There were mild symptoms of thirteen years' duration, with an acute flare-up following a trauma one month previously. The floor of the subacromial bursa was smooth and glistening except for one localized reddened area (fig 4). The deposit extended proximally within the substance of the tendon 1 inch (2.5 cm) from its insertion. It was continuous through a sinus tract with a calcareous mass which had dissected downward to elevate the floor of the bursa for approximately 2 inches (5 cm). Sections are shown in figures 3, 4 and 5.

14 Brickner, W. M. Prevalent Fallacies Concerning Subacromial Bursitis: Its Pathogenesis and Rational Operative Treatment, *Am J M Sc* **149** 351-364, 1915, Pain in the Arm, Subdeltoid (Subacromial) Bursitis: A Further Study of Its Clinical Types, Pathology and Treatment, *J A M A* **69** 1237-1243 (Oct 13) 1917.

or hard according to the duration of the process. In the earlier stages their substance is little more than a milky fluid and resembles staphylococcus pus. With the lapse of time, the fluid is gradually absorbed, in most cases the deposits have the consistency of ointment and will exude in the form of a ribbon as if under pressure, when the overlying tendon fibers are split. After a number of months or even years, further



Fig. 3—Multiple calcareous deposits embedded in the hyaline connective tissue which fills the defect between the ruptured fibers of the supraspinatus tendon. Note the rounded calcified areas which have pushed the connective tissue before them as they enlarged. The roentgen appearance is shown in figure 2.

inspissation renders the deposit rather granular, dry, chalklike and finally gritty.

These deposits may occur as a number of foci (fig. 3). In 1 instance from microscopic study of a surgical specimen, Carnett and Crue

estimated that from 500 to 1,000 such areas were present. These varied from microscopic to considerable size. The larger accumulations, particularly when fluidlike, may produce an elevation under the base of the bursa resulting from localized swelling of the underlying tendon.

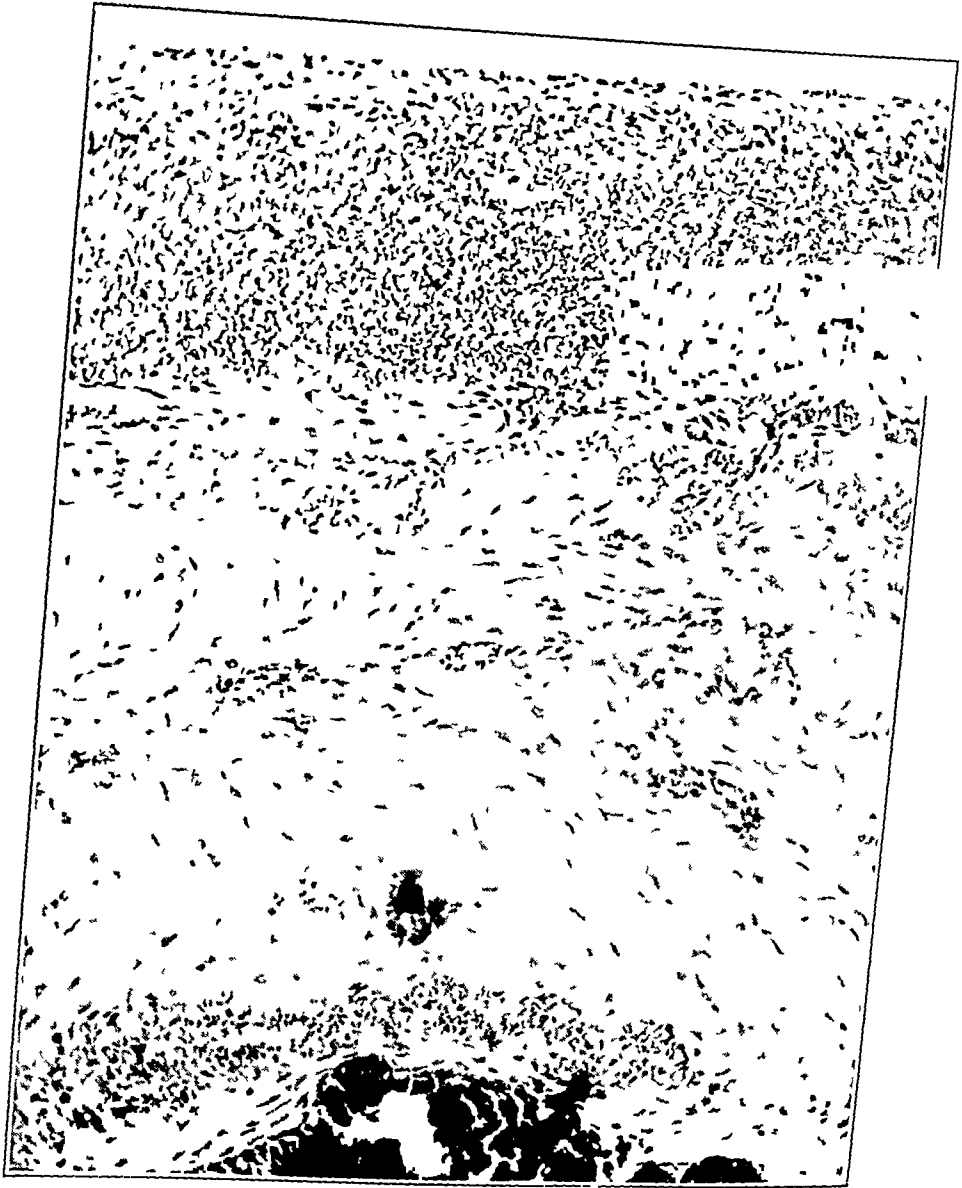


Fig. 4—Calcified mass in the supraspinatus tendon, surrounded by hyaline connective tissue and showing a relatively normal overlying bursal floor. Note the subsynovial reaction to the mechanical irritation. The specimen was taken from the localized reddened area at the base of the bursa. The roentgen appearance is shown in figure 2.

Rarely, the deposits rupture into the bursa, producing chemical bursitis with effusion.

In reporting the microscopic observations in sections of the supraspinatus tendon from 31 shoulders, Case stated that he found cartilage in several (fig 5) and true bone formation in 1. The local reaction varies in degree from the extensive formation of granulation tissue to the scattered infiltration of a few cells. As the lesions are noninfectious, there appears to be little attraction for polymorphonuclear leukocytes. Lymphocytes, plasma cells and large mononuclear wandering cells are the ones usually encountered (fig 4), but in many instances foreign body giant cells may be seen. With this cellular infiltration the fixed

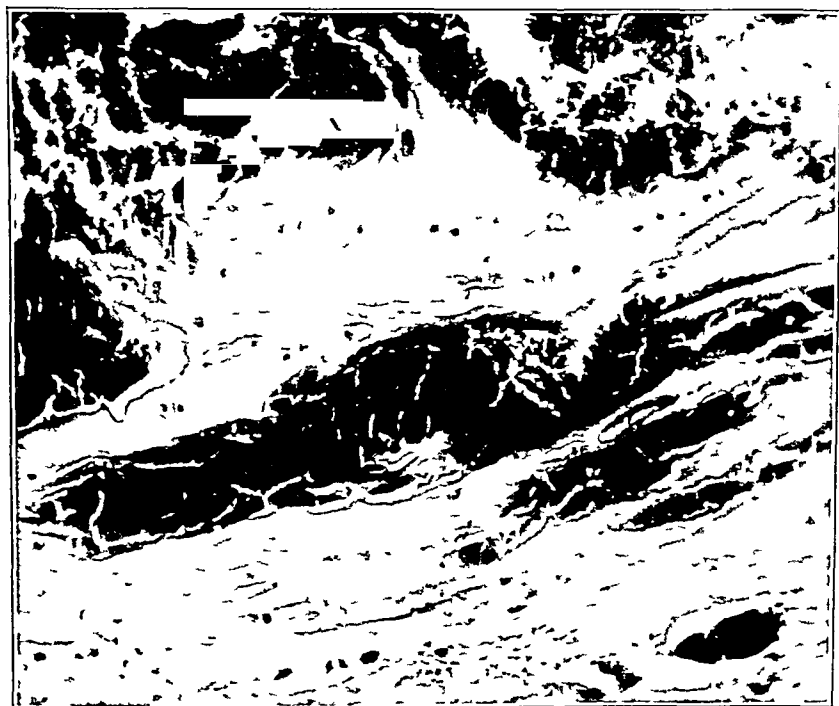


Fig 5—Multiple areas of calcification within the substance of the supraspinatus tendon. Note the metamorphosis of hyaline connective tissue to cartilage and the absence of a limiting membrane about the deposits, which in this area were brittle and chalklike. This is believed to represent a deposit of long standing.

tissue cells respond by proliferation, adding the fibroblast in few or greater numbers to the cellular ensemble to give a typical reaction such as would occur in the presence of any foreign substance.

The symptoms presented in general bear no relation to the size or duration of the deposit or to the amount of inflammatory reaction at the base of the subacromial bursa. It is generally believed that the deposition of the lime salts precedes by weeks, months or even years the

onset of clinical symptom. After the deposit has formed, a mild trauma may incite acute inflammation with rapid development of the clinical symptoms, which probably result from the rupture of a few of the adjacent tendon fibers. The acute inflammation, with its increased blood supply and accumulation of inflammatory cells (fig. 4), "steps up" the local metabolic rate, with subsequent production of carbon dioxide in sufficient amount to lead gradually to dissolution of the calcareous deposit. The stiffness and limitation of motion accompanying this condition are due to pain and associated muscle spasm in the acute phase but in the chronic phase they are due to contracture of the muscles and ligaments about the shoulder, which results from the prolonged voluntary fixation.

SYMPTOMS

The group of conditions responsible for disability of the shoulder joint have much in common when one is considering the onset and course of the lesion and, if not carefully studied, will seem so similar that a differential diagnosis will be impossible.

Occasionally the onset of symptoms is abrupt and viciously painful but a detailed inquiry in most cases will elicit the history of an insidious beginning. Usually, two, six or more months before the acute onset it is noticed that there is an uncomfortable feeling associated with certain movements of the shoulder—abduction and internal rotation. Some patients find that it is uncomfortable to lie on that side and that the most comfortable position for rest is on the back, with the forearm of the troublesome side above the head, others learn to abduct the arm slightly on a pillow. Later there is a definite painful "hitch" associated with abduction of the arm through the arc from 70 to 100 degrees.

The usual sequence of events leading to an acute attack is some type of work which places an abnormal strain on the shoulder, painless at the time but recalled when symptoms develop. However, the following morning the shoulder is stiff and extremely painful on all motions. A minor trauma to the shoulder, apparently insignificant, may incite the same train of symptoms.

An acute attack may be brought about in the same way without previous subjective symptoms. Rarely, a patient cannot recall either antecedent trauma or previous symptoms of any kind.

Pain—The pain suffered by patients with calcified deposits in the region of the shoulder should be grouped into three types, which may appear singly or in combination and may vary in degree from mild to agonizing.

It has long been recognized that many patients suffering from inflammatory conditions about the subacromial bursa feel pain only at the point of insertion of the deltoid muscle. This pain is described as sharp, cutting

or stabbing and has been compared to the pain which accompanies motion in an arthritic joint

A greater percentage of the patients complain of a constant dull, boring or aching pain localized to the tip of the shoulder at the point of greatest tenderness. It results from accumulation of serum and inflammatory products about the deposit, which increases the pressure within the tendon and stretches the overlying synovial membrane.

There is a third type of pain associated with this and other lesions about the shoulder, which has not been overlooked but which has never been accorded its proper significance. At any time during the stage of acute or subacute symptoms the patient may suffer almost intolerable pain in the muscles of the neck, in the scapular region and occasionally down the arm as far as the finger tips. Most often it follows the distribution of the ulnar nerve, but occasionally it is encountered in the areas innervated by the median and radial nerves. It is described as shooting and burning in nature. At times there is numbness like the sensation experienced when an extremity "goes to sleep." Not infrequently there is also swelling of the involved hand. Sensory and other subjective neurologic changes are not uncommon. These findings, composing a syndrome heretofore referred to as "brachial neuritis," are identical with those encountered in the "scalenus anticus syndrome"¹⁴¹ and are believed to result from reflex spasm of the scalenus anticus muscle of the affected side.

DIAGNOSIS

From the foregoing review of the anatomy, etiology, pathology and symptomatology of these lesions of the shoulder, it can be seen that the diagnosis depends on a carefully taken history and on the physical findings. According to the symptoms, the duration of the subjective complaints and the severity of the pain with its associated muscle spasm and limitation of motion, the physical signs vary from case to case and in the same patient from day to day.

With the arm by the side, palpation will reveal a localized area of maximum tenderness below the tip of the acromion which often coincides with an area of swelling. This may be accurately localized with reference to the bicipital groove, provided the symptoms are not too acute. There will be a painful "hitch" on abduction and again on descent of the arm. Also, on abduction the tender area will disappear beneath the tip of the acromion, a sign described by Dawbarn¹⁵ in 1906. Abduction and rotation will be limited but the other motions usually are essentially normal.

141 Ochsner, A., Gage, M. and DeBakey, M.: Scalenus Anticus (Naffziger) Syndrome, *Am. J. Surg.* **28**: 669-695, 1935.

15 Dawbarn, R. H. M.: Subdeltoid Bursitis—A Pathognomonic Sign for Its Recognition, *Boston M. & S. J.* **154**: 691, 1906.

However, the question of whether a calcareous deposit is present in any given case can be settled only by an adequate roentgen examination. When the calcified mass lies over the summit of the humerus (fig 6), it may be lost in the superimposed shadow of the posterior portion of the acromion and the head of the humerus when the usual technic with the tube directly in front of the shoulder is employed. Carnett³ has shown that deposits in this location can be thrown into relief between the acromion and the humeral head by directing the central ray slightly caudad and laterally—usually 10 to 15 degrees from the vertical in each direction.

The more usual location of these calcareous masses near the insertion of the tendons, however, presents a different problem. With this in mind the subacromial bursa was opened to allow pieces of lead to be accurately placed between the tendon fibers. Roentgenograms were then taken with the arm in various positions. As is shown in figure 6 the importance of securing roentgenograms with the humerus in different degrees of rotation cannot be overemphasized.

Even when the position would demonstrate the deposit in silhouette, overexposure or overdevelopment will demonstrate only shadows of the more dense areas. It is therefore suggested that a "semisoft" technic be employed routinely in roentgen examination of the shoulder. This will reveal a shadow of the deposit if it is present and will also show any departures from normal in the surfaces of the adjacent bone. If stereoscopic views of the shoulder are desired, two exposures with the humerus in the neutral position and a third with the humerus in lateral rotation will prove satisfactory.

TREATMENT

In considering the treatment of patients suffering from calcareous deposits about the shoulder, one should classify the lesions into two types, the acute and the chronic. If there is a sudden onset of pain localized at the point of the shoulder and present even when the arm is at rest, the condition should be treated immediately by lavage, as advocated originally by Smith-Petersen and his associates. In the less severe attacks the patient may be kept comfortable with sedatives and an ice bag to the shoulder until the acute process has subsided. When the subacute, or chronic, stage is reached, a decision must be made to give diathermy or roentgen therapy a trial or to resort to lavage if it has not been used previously.

It must be emphasized that, although lavage may not remove completely the calcareous mass, the mechanical irritation produced by the needle usually results in infiltration of inflammatory cells, which increases the local metabolism and results in absorption of the deposit. The

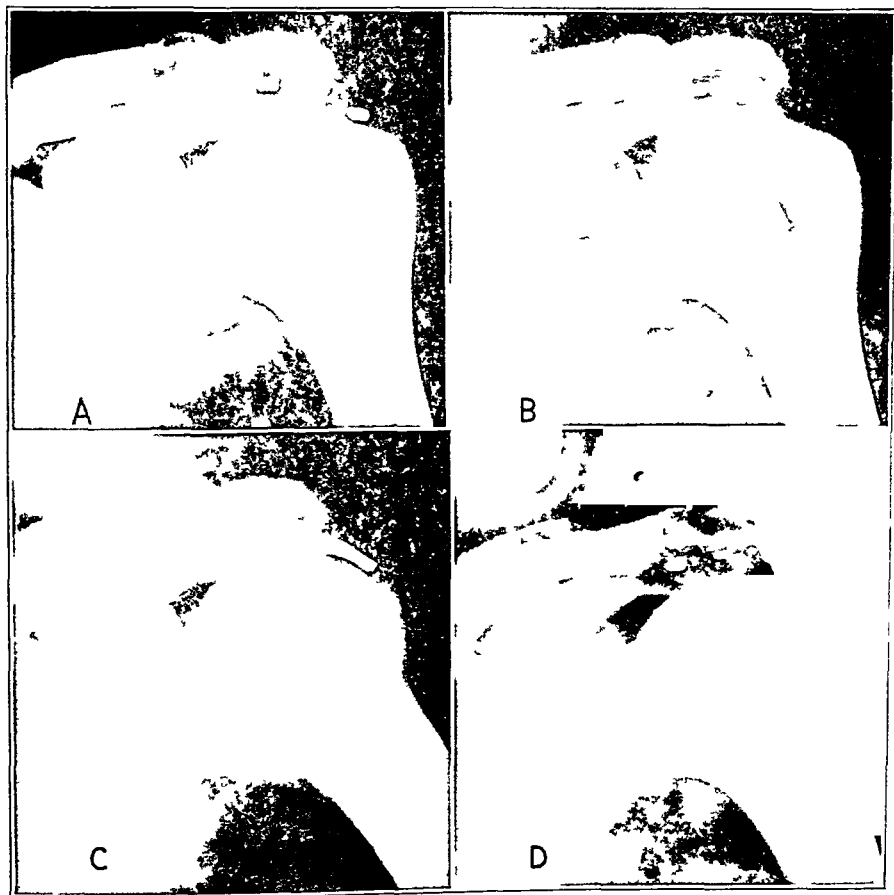


Fig 6—*A*, roentgenogram showing lead markers within the substance of the supraspinatus tendon, one at its insertion and the other 1 inch (2.5 cm) proximal. The arm is in the neutral position with reference to rotation. Note the superimposed shadow of the proximal marker and the acromion. The shadow of the distal marker is thrown in silhouette. *B*, roentgenogram showing the proximal lead marker in the supraspinatus tendon as in *A* and another at the insertion of the subscapularis tendon. Note the superimposed shadows of the marker in the subscapularis tendon and the head of the humerus when the arm is in the neutral position. *C*, same as *B* except the arm is in external rotation. Note the shadow of the marker at the insertion of the subscapularis tendon in this position as compared to *B*. *D*, roentgenogram taken with the shoulder in the neutral position. Note the shadow of the lateral marker which was placed between the fibers of the infraspinatus tendon near its insertion. The proximal marker is within the supraspinatus tendon.

immediate relief often experienced by the patient probably results from the release of tension within the tendon.

In a relatively small percentage of cases the calcification and the resultant symptoms cannot be satisfactorily treated without surgical removal. This may be performed through a short exploratory incision with the region under local anesthesia.

REPORT OF A CASE

D. R., a Negress aged 37, a housewife, was referred to the Cincinnati General Hospital on Oct. 7, 1937, from the orthopedic clinic because of severe pain in the left shoulder, arm and hand.

She described the onset of a tingling and "puffed-up" sensation in her left hand about six months previously. At that time there was no discomfort in the shoulder, but after about two months she began to feel a sharp, stinging pain in the region of insertion of the deltoid muscle on elevation of the arm. Soon thereafter, lying on the affected side produced enough discomfort in the shoulder to prevent sleep. By two months before admission she had discovered a tender point at the tip of her left shoulder, where a constant dull, boring and throbbing pain was present. This was so severe at night that she slept little. It gradually grew worse, being so severe that she paid little attention to the numbness and tingling in her hand. From six weeks before admission, her left hand would regularly swell at night, the swelling disappearing during the day. She stated that she often dropped dishes or other household articles picked up with the left hand because she "could not feel them." This resulted in great anxiety, she feared that she was becoming paralyzed.

Two weeks previously, the increased pain and helplessness forced her to give up work. She sought relief by attending the medical clinic, where she was being treated for obesity. At that time her chief complaint was swelling of the left arm and hand, accompanied by numbness and tingling beginning at the left shoulder and extending down the arm to the finger tips. The general physical examination otherwise gave negative results. A diagnosis of scalenus anticus syndrome was made.

Orthopedic consultation revealed limitation of abduction and of rotation at the left shoulder by more than one half. Any movement of the joint produced pain at the point of the shoulder, where there was a localized area of tenderness just lateral to the bicipital groove. Muscular power in the left arm was weaker than in the right. The left forearm and hand were swollen, and there was diminution of sensation over the entire arm, forearm and hand to pinprick, point discrimination, heat and cold. This diminution was most pronounced over the ulnar distribution. Stereognostic sense was impaired, so that the patient could not recognize a fountain pen, a door key, a safety pin or a coin, all of which were readily identified in the right hand. There were definite tenderness and fulness in the angle between the sternocleidomastoid muscle and the clavicle on the left.

The diagnosis was changed to calcification of the left supraspinatus tendon, with spasm of the scalenus anticus muscle. Diathermy treatments were started, and roentgenograms of the shoulder and the cervical portion of the spine were taken. They did not reveal cervical rib but showed a shadow in the region of the left shoulder, just above the greater tuberosity (fig. 1). Ten days later, she had not improved with diathermy treatments and was referred to the hospital.

On admission the findings were essentially unchanged. Her chief complaint was a sensation of puffiness and numbness associated with swelling of the left hand and accompanied by sharp, burning, shooting or tingling pains down the distribution of the ulnar nerve to the finger tips. Neurologic consultants agreed with the findings and made a diagnosis of scalenus anticus syndrome. Vascular examination revealed that the left hand was 2 degrees warmer than the right and that the change in temperature with heating was greater on the left. In addition oscillometric tracings revealed that heating resulted in the normal changes on the right but had little effect on the left.

With the region under local anesthesia, an exploratory incision was made into the subacromial bursa. When the humerus was rotated, the greater part of its floor could be inspected and was found to be entirely normal except for an elevation just lateral to the bicipital groove and just above the insertion of the supraspinatus tendon. On incision the calcareous deposit was found to have the consistency of cottage cheese and escaped as it under pressure. Biopsy showed a deep-staining calcium deposit embedded in an area of hyaline connective tissue entirely within the substance of the tendon.

The swelling of the hand, pain in the arm and sensory changes, as well as the fulness and tenderness in the region of the left scalenus anticus muscle, disappeared within a few hours after the operation and did not return. By the fourth post-operative day motion was greater than on admission and was painless. The patient was still asymptomatic seven months after the operation.

Comment—This report represents 1 of 11 recent similar cases of a rather typical scalenus anticus syndrome in which the condition was entirely relieved by treatment of the calcification of the supraspinatus tendon.

SUMMARY AND CONCLUSIONS

No attempt has been made to discuss a differential diagnosis of lesions of the shoulder except in connection with cases in which calcareous deposits are present. As was shown by Codman, such deposits are most often located in the tendon of the supraspinatus muscle at the usual site of rupture, near its attachment into the greater tuberosity of the humerus. Occasionally the tendon of the infraspinatus or the subscapularis muscle is involved. The calcium salts are thought to be laid down slowly over a period of months or even years in the hyaline connective tissue subsequent to repair of repeated minor traumas. The masses are asymptomatic until they are large enough to produce mechanical disturbances or until a minor trauma tears a few of the adjacent tendon fibers and produces mechanical irritation with the accumulation of serum and inflammatory cells to activate the process.

A case is presented to illustrate the types of pain encountered. Pain in the region of the insertion of the deltoid muscle is thought to be referred from the subacromial bursa. The increased pressure within the tendon and the stretching of the overlying synovial membrane which lines the base of the bursa seem to account for the occurrence of constant dull boring or aching pain localized to the point of the shoul-

der. The third type of pain encountered in this condition is really the result of a complication. It consists of pain throughout the distribution of the brachial plexus. The most severe symptom is a burning, shooting or tingling sensation down the arm, most often in the distribution of the ulnar nerve but also encountered in the areas innervated by the median and radial nerves. It is often associated with swelling of the involved hand. Oscillometric tracings may show some decrease in the vascular pulsations on the affected side. Sensory and other subjective neurologic changes are not uncommon. The entire picture is that presented by the scalenus anticus syndrome and is thought to result from reflex spasm of the scalenus anticus muscle of the affected side.

The diagnosis depends on a carefully taken history and on the physical findings, which, however, differ little from those associated with other painful conditions of the shoulder. Roentgen examination should consist of the taking of anteroposterior views of the shoulder with the humerus in the neutral position and in lateral rotation, a "semisoft" technic being advisable.

Routine treatment is considered radical. The acute condition should be treated immediately by lavage. In the subacute or chronic stages, a decision must be made to give diathermy a trial or to resort to lavage if it has not been used previously. In a small percentage of cases the condition cannot be satisfactorily treated except by surgical removal of the deposit.

The cases mentioned in this report were studied under the supervision of Dr. J. A. Freiberg.

ACUTE PANCREATIC NECROSIS AND ACUTE INTERSTITIAL PANCREATITIS

TREATMENT WITHOUT OPERATION A CLINICAL STUDY OF TEN CASES

MELVIN A CASBERG, M D
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Acute pancreatic necrosis is a term usually applied to a serious, often fatal, disease of the pancreas which is due to autodigestion of the gland, presumably by activation within the ducts of trypsinogen to trypsin, the latter being a powerful proteolytic ferment. The classic observations of Fitz,¹ based on necropsy study, have long been the basis for physicians' knowledge of this remarkable condition. The mortality is very high even if operation is carried out, although it has been generally agreed that the disease is primarily surgical and that surgical intervention offers the greatest hope of survival.

For the past decade or so a growing experience has shown that many patients with acute pancreatitis are cured without operation and that many are cured even if nothing more than exploration is done at operation. According to this point of view, acute pancreatitis tends to become less and less a surgical disease, in the sense that operation is not indicated and may even prove deleterious. Although the pendulum is thus swinging from operative to nonoperative therapy, there is good reason to suspect that the true state of affairs lies somewhere between the two extremes. This has been suggested by evidence indicating that there are two types of acute pancreatitis, one a self-limited inflammation or obstruction which subsides spontaneously and has been designated as acute interstitial pancreatitis and the other, which is the serious, often fatal, type, being most appropriately described as acute pancreatic necrosis.

The present clinical study is based on 5 cases of each type in all of which the condition was primarily treated without operation. The differences between the two groups were so striking that it seemed worth while to summarize them with the view of suggesting a form of

From the Surgical Unit of the Washington University School of Medicine
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1 Fitz, R. H. Acute Pancreatitis. A Consideration of Pancreatic Haemorrhagic, Suppurative and Gangrenous Pancreatitis and of Disseminated Fat-Necrosis, Boston M. & S. J. 120 181-229, 1889

therapeutic approach that might tend to lower the mortality, which in the cases of acute pancreatic necrosis was 100 per cent

In the first 5 cases reported, the diagnosis was acute interstitial pancreatitis; in the second group, acute pancreatic necrosis

REPORT OF CASES

CASE 1—A 42 year old Armenian man entered the hospital on Dec 14, 1937, complaining of severe epigastric pain with a fairly sudden onset forty-eight hours prior to entry. The pain was constant and did not radiate. The patient vomited once and had several watery stools after self medication with "salts". There was no history of jaundice. He had had one similar attack six months previously, milder than the present one.

Physical Examination—The patient was well nourished, swarthy and somewhat obese. He appeared rather acutely ill. There was no visible evidence of jaundice. The abdomen moved freely with respiration, and there were no visible masses. Palpation of the abdomen showed tenderness and voluntary muscle guard over the epigastrium and the right upper quadrant. There was no rigidity. No masses were felt.

Laboratory Examination—The urine gave a 1 plus reaction for albumin but contained no sugar. The leukocyte count was 14,000 per cubic millimeter. The Kahn reaction was negative. The value for sugar was 114 mg and that for non-protein nitrogen 24 mg per hundred cubic centimeters of blood (both normal). The value for blood amylase on December 14 at 6 p. m. was 200, at 11 p. m. the same day it was 250. On December 15 it was 250. On December 16 and 17 it returned to normal, i. e., 33 and 30, respectively. The icterus index remained normal.

A roentgenogram taken on December 14 disclosed no free air under the diaphragm. One week after the patient's admission a cholecystogram taken after intravenous injection of soluble iodophthalein U. S. P. revealed a pathologic gall-bladder (no shadow).

Course—The patient improved steadily with a diet high in carbohydrates. Two days after admission he was free from symptoms. Cholecystectomy was advised, but he refused the operation and left the hospital.

Two months later he was readmitted, with complaints similar to those noted at the time of his first entry, plus radiation of the epigastric pain to the back. The attack had commenced eighteen hours prior to entry. The value for blood diastase, determined twenty-four hours later, was 67, and forty-eight hours later it was 33, the latter value being normal. Three days after admission, all acute symptoms having subsided, an abdominal exploration was performed, and the pancreas was said to be acutely injected but fairly normal to palpation. The gall-bladder was fibrotic and adherent. No stones were found in the common bile duct, which was not dilated. A cholecystectomy was performed, and the common duct was drained by a T tube. A biopsy of pancreatic tissue taken at the time

2 Chemical methods were standard except for that used to determine the amylase content of the blood, which was the procedure recently described by M. Somogyi (Studies on Blood Diastase, *Proc Soc Exper Biol & Med* 29 1126 1128 [June] 1932, Blood Diastase as Indicator of Liver Function, *ibid* 32 538-540 [Dec.] 1934)

of operation revealed marked fibrosis of the interacinar framework and some infiltration with lymphocytes. There was no necrosis or suppuration. The pathologic diagnosis was chronic pancreatitis. The liver showed considerable fatty degeneration, the gallbladder revealed only slight change.

CASE 2—A white woman aged 60 entered the hospital on April 30, 1937, complaining of severe pain in the epigastrium and both upper quadrants of the abdomen which radiated to the back along both costal margins. The onset had taken place about six hours before entry and the patient had vomited several times. She described similar previous attacks which were milder, though sequentially increasing in severity.

Physical Examination—The patient was very obese and acutely ill. Tenderness was elicited across the entire upper part of the abdomen. There were no palpable masses and no muscle guard. There was no jaundice.

Laboratory Examination—The urine showed no albumin or sugar. The leukocyte count was 8,640 and the erythrocyte count 3,800,000 per cubic millimeter of blood. The Kahn reaction was negative. The value for blood sugar was 122 mg and that for nonprotein nitrogen was 21 mg per hundred cubic centimeters. The value for blood amylase on May 1 was 333 in the morning and 225 in the afternoon. On the two successive days the values had fallen to 182 and 28 respectively.

Course—Three days after admission all symptoms had subsided and the patient was discharged.

CASE 3—A white man aged 65 entered the hospital on June 29, 1937, complaining of severe epigastric pain which had begun six hours prior to entry and was steadily becoming worse. The patient was nauseated and vomited several times. He had had several similar attacks before this, one accompanied by jaundice in 1935. The patient was being treated by a private physician for "ulcer of the stomach."

Physical Examination—The patient was well nourished. He was in acute distress. There was visible jaundice. Palpation over the epigastrium was painful. There was some tenderness in both subcostal areas particularly on the left. There was no rigidity, and no masses could be outlined.

Laboratory Examination—The diastase content of the urine was 4,000, otherwise the urine was normal. The value for blood sugar was 158 mg and that for nonprotein nitrogen was 27 mg per hundred cubic centimeters. The leukocyte count was 7,100 per cubic millimeter. The Kahn reaction was negative. The icterus index was 50. The blood amylase on the morning of June 29 was 400 and on the afternoon of the same day was 500. On June 30 and July 2 the figures had dropped to 165 and 20, respectively.

Roentgen examination for free air under the diaphragm gave negative results at the time of the patient's admission and on July 9 a cholecystogram taken after intravenous injection of soluble iodophthalein U. S. P. was normal.

Course—Three days after the patient's admission the symptoms had subsided and six days later he was discharged.

CASE 4—A white man aged 69 entered the hospital on Dec. 2, 1935, complaining of severe pain in the midline just above the umbilicus. The onset had taken place one week previously and had been accompanied with jaundice. There was no history of radiation of pain. The condition had become progressively worse.

until the patient sought hospitalization. He was nauseated and vomited frequently. There was a history of previous attacks, milder than the present episode.

Physical Examination—The patient was well developed and well nourished. There was an icteric tinge to the skin. The abdomen was obese and tender to palpation over the epigastrium and the right upper quadrant of the abdomen. There was no rigidity, and the examiner described a "vague mass in the right upper quadrant."

Laboratory Examination—The urine showed a trace of albumin and gave a strongly positive reaction for bile. The leukocyte count was 24,200 and the erythrocyte count 5,360,000 per cubic millimeter. The Kahn reaction was negative. The value for sugar was 99 mg and that for nonprotein nitrogen was 35 mg per hundred cubic centimeters of blood. The amylase content of the blood on December 4 (thirty-six hours after admission) was 110, and on the next day it was 25. The icterus index was 90.

Past History and Course—Fifteen months prior to this entry the patient had been hospitalized because of a similar attack. His condition was diagnosed as cholecystitis, and roentgenograms of the gallbladder taken after intravenous injection of soluble iodophthalein U S P (Sept 27, 1934) showed pathologic functioning. The patient was discharged five days after entry.

CASE 5—A white woman aged 27 entered the hospital on Aug 7, 1936, complaining of extreme pain in the epigastrium, nausea and vomiting which began about thirty-six hours prior to entry. The pain was persistent and stabbing, frequently radiating to the interscapular region. No history of jaundice was obtained. The patient had had two previous attacks within four months previous to hospitalization.

Physical Examination—The patient was moderately obese. She was in acute distress. Palpation revealed fulness in the epigastrium with tenderness confined to the region of the pancreas and a typical "Head" zone of cutaneous hyperesthesia. There was voluntary muscle guard over the entire upper part of the abdomen, but there was no rigidity.

Laboratory Examination—The urine gave a 2 plus reaction for albumin but was otherwise normal. The leukocyte count was 20,400 per cubic millimeter on the patient's admission and 8,900 six days later. The Kahn reaction was negative. The value for blood sugar was 155 and that for nonprotein nitrogen was 24 mg per hundred cubic centimeters. The amylase content of the blood on the day of admission was 330, on the following seven successive days it fell to 160, 115, 15, 18, 20, 28 and 20. The icterus index was normal.

Roentgen examination of the gallbladder after intravenous injection of soluble iodophthalein U S P revealed it to be pathologically functioning (no shadow).

Course—The patient's symptoms had subsided three days after admission, and on August 26 a cholecystectomy was performed. There were many stones in the gallbladder. The common duct showed no changes, the pancreas was not examined. The patient died on the fifth postoperative day. Permission for autopsy was refused.

CASE 6—A white man aged 61 entered the hospital on Dec 11, 1935, complaining of severe epigastric pain of five hours' duration. The pain was persistent. It did not radiate to the back but was accompanied by nausea and vomiting. There was no history of a similar attack, and the patient stated that he had never had jaundice. There was a history of cardiac disease and digitalization.

The patient was not in acute distress. The heart was enlarged, the sounds were irregular. The abdomen moved with respiration and was moderately distended. The liver was enlarged. There was tenderness in the epigastrium and to a lesser degree in both upper quadrants of the abdomen. Voluntary muscle guard over the entire upper part of the abdomen was encountered, but there was no rigidity.

Laboratory Examination—The urine was essentially normal. The leukocyte count was 7,400 per cubic millimeter. The Kahn reaction was negative. The value for blood sugar was 90 mg and that for nonprotein nitrogen 38 mg per hundred cubic centimeters. The amylase content of the blood on December 12 was 200 both in the morning and in the afternoon. The following day it fell to 166. December 16, 18, 21 and 23 the readings were 10, 30, 40 and 28, respectively. The icterus index was 75.

A roentgenogram taken on admission showed no free air under the diaphragm.

Course—The patient became progressively worse, the symptoms being localized in the epigastrium and the right upper abdominal quadrant. The white blood cell count was elevated to 43,000 on December 23 and on the evening of the same day, twelve days after admission, the patient died.

Postmortem Examination—The chief cause of death was acute necrotic pancreatitis. There was a large amount of free purulent fluid within the abdominal cavity, and the peritoneum and mesentery were studded with chalky areas of necrosis, with numerous pockets of pus and debris between adherent loops of intestine. The omentum was thick and friable. The liver was not enlarged but gave microscopic evidence of chronic hepatitis. The gallbladder was filled with small stones and purulent bile, and the cystic and common ducts were dilated, the latter containing about a dozen small faceted stones. The pancreas was swollen, necrotic and black. The pancreatic duct was patent and bile stained. Microscopically, whole sections of the pancreas were necrotic, with some round cell infiltration into the bordering tissues.

CASE 7—A white woman aged 81 entered the hospital on March 19, 1937, complaining of generalized abdominal pain, nausea and vomiting of three days' duration. The pain was most marked in the epigastrium, and the patient stated that it did not radiate. There was no history of similar previous attacks.

Physical Examination—The patient was in acute distress. She was cyanotic and had a grayish pallor. The abdomen moved with respiration and was not rigid. There were no bowel sounds. The upper part of the abdomen was tender and exhibited voluntary muscle guard.

Laboratory Examination—The urine gave a 1 plus reaction for albumin. The leukocyte count was 13,800 per cubic millimeter. The Kahn reaction was negative. The value for blood amylase was not determined.

Course—The patient became progressively worse and died on the day after admission. The diagnosis was partial intestinal obstruction.

Postmortem Examination—The main cause of death was acute pancreatic necrosis. Grossly, the distal two thirds of the pancreas was entirely necrotic and hemorrhagic. The peritoneal cavity contained several hundred cubic centimeters of bloody fluid. The gallbladder was moderately distended and contained about fifteen small stones. The common bile duct was slightly dilated but contained no stones. The main pancreatic duct was patent and contained no calculi or bile. Microscopically, a section through the head of the pancreas showed little change.

except some round cell infiltration into the peripancreatic fat. Sections from the body and tail of the pancreas revealed complete destruction of pancreatic tissue.

CASE 8—A white woman aged 33 entered the hospital on Nov. 1, 1937, complaining of abdominal pain, nausea, vomiting and chills. The patient had been feeling "under par" for three weeks but noticed the severe abdominal pain only four days prior to entry. She also complained of repeated chills and of burning on urination.

Physical Examination—The patient was moderately obese. She was in shock. The pulse was rapid and thready. The skin was cold, and the temperature was subnormal. There were tenderness and voluntary muscle guard over the entire abdomen, most marked in the upper quadrants. There was marked tenderness in both costovertebral angles. The chest was essentially normal.

Laboratory Examination—The urine gave a 3 plus reaction for albumin. The leukocyte count was 26,350 per cubic millimeter. The Kahn reaction was negative. The value for sugar was 252 mg. and that for nonprotein nitrogen 42 mg. per hundred cubic centimeters of blood. The value for blood amylase was not determined.

Course—Two days after admission the patient had a sudden fairly severe hemoptysis, and the entire chest revealed moist, coarse rales on auscultation. Roentgenograms taken with an emergency portable apparatus at the bedside revealed blotchy areas of consolidation over both lung fields, suggestive of extensive bronchopneumonia or acute pulmonary edema. The patient died three days after admission, and a diagnosis of tuberculous pneumonia was made.

Postmortem Examination—The prime cause of death was acute pancreatic necrosis. The lungs showed no pneumonic process but were edematous. The peritoneal cavity contained about 250 cc. of straw-colored fluid. The gallbladder and bile ducts appeared normal. Grossly, the entire pancreas contained fatty necrotic areas and multiple hemorrhagic spots. The ducts showed no calculi or evidence of dilatation. Microscopically, all sections showed extensive necrosis, even the supportive structures in some areas were unrecognizable.

CASE 9—A white man aged 34 entered the hospital on June 10, 1936, and was sent to the ward for patients with alcoholism because of a strong alcoholic odor to his breath. He gave a history of heavy imbibing of alcoholic beverages during the past ten days. However, two days prior to entry he noticed pain and distention in the upper part of the abdomen and was thereafter unable to retain either food or water. There was no history of radiation of pain or of previous attacks. His bowels had been moving rather loosely.

Physical Examination—The patient was moderately obese. He was sitting up in bed. He was moderately dyspneic. He was conscious and rational but rather apprehensive. The abdomen was distended but showed no rigidity. There was considerable tenderness over the right upper quadrant, and the edge of the liver was palpated slightly below the right costal margin. Voluntary muscle guard was present over the upper part of the abdomen. No abnormal masses were palpated. Shifting dullness and a fluid wave were demonstrated.

Laboratory Examination—The urine gave a 4 plus reaction for albumin and for urobilinogen. The leukocyte count was 4,600 and the erythrocyte count 3,920,000 per cubic millimeter. The Kahn reaction was negative. The value for sugar was 149 mg. and that for nonprotein nitrogen was 23 mg. per hundred cubic centimeters of blood. The icterus index was 75. The value for blood amylase was not determined.

Course—The patient became progressively worse. On November 13, three days after admission, he went into shock and died. The diagnosis was alcoholic enteritis.

Postmortem Examination—The cause of death was acute pancreatic necrosis. The peritoneal cavity contained about 500 cc of bloody fluid, and there were numerous chalky white areas of fat necrosis on the surface of the greater omentum. The liver was enlarged and showed evidence of fatty degeneration. The gallbladder was adherent to the omentum and on pressure expelled bile through the ampulla of Vater. In the region of the pancreas there was a large, dark red friable mass surrounded by omentum. There was considerable fat necrosis about the pancreas. The main duct was patent and contained no stones. Microscopic section showed the tail to be entirely necrotic; the body and head showed fairly normal acinar tissue with fat necrosis in the interacinar fibrous tissue.

CASE 10—A white man aged 42 entered the hospital on June 16, 1936, complaining of pain in the epigastrium, nausea and vomiting. At the onset, which had taken place two days prior to entry, the pain was not severe, but four hours later it became alarming and a physician was called in. He described the pain as commencing in the epigastrium, radiating to the right and finally including the entire abdomen. The patient vomited about twelve times. No history of any similar previous attack was reported. There was a vague history of jaundice.

Physical Examination—The patient was obese. He was in acute distress and in mild shock. The abdomen was distended but not rigid. Tenderness was elicited in the epigastrium and in the right upper quadrant. A large mass was palpated across the epigastrium.

Laboratory Examination—The urine on admission was essentially normal. The leukocyte and erythrocyte counts were 16,350 and 5,050,000 per cubic millimeter, respectively. The Kahn reaction was negative. The value for blood sugar was 213 mg. and that for nonprotein nitrogen was 63 mg. per hundred cubic centimeters. The value for blood amylase was 20 and remained normal or low throughout the disease. The icterus index was 63. The organism in the culture of material taken from the abdominal cavity at the time of operation was reported as *Staphylococcus albus*.

Course—The patient slowly improved under treatment with a conservative regimen plus blood transfusions. On July 8 the following notes were made by the resident: "Patient still presents the picture of chronic illness. Has a large mass in the upper part of the abdomen. Believe this is a condition which originated with disease of the gallbladder and went on to cause acute pancreatitis. Believe the patient had a localized peritonitis or abscess in the lesser peritoneal cavity, which then extended to the right to give a subphrenic abscess. This seems to be confirmed by a roentgenogram of the chest which shows a high elevation of the diaphragm on the right. Two days previously the patient began to complain of severe pain in the left lower part of the chest. Examination revealed a loud, rough friction rub."

On July 12, the patient had been in the hospital over three weeks and an exploratory laparotomy was performed. This revealed a large fairly well walled-off abscess which extended beneath the liver and also communicated with a similar process over the pancreas. On July 15, after a rather stormy postoperative course the patient died.

Postmortem Examination—There was a large abscess cavity beneath the liver, which was well walled off from the greater peritoneal cavity. The abscess extended

into the lesser peritoneal space and retroperitoneally, where it enclosed the pancreas. It contained a mass of necrotic friable material the structure of which resembled that of the pancreas. The liver was normal in size and shape, and there was no evidence of subdiaphragmatic abscesses. The common bile duct and the gallbladder showed normal patency and contained no stones. Microscopically the pancreas revealed large areas of edematous necrotic tissue. There were also large areas of uninvolved pancreas, and in these regions considerable fibrosis was observed.

COMMENT

The data presented in this report are really self explanatory. Much of the significant material has been summarized in the accompanying chart and table. Further presentation of the findings will be correlated with a brief discussion of the problem as well as a review of the recent literature under appropriate headings.

Classification—Until 1933 the term acute pancreatitis meant in general but one disease, namely, the acute fulminating type of pancreatic necrosis. At that time, Elman³ presented evidence, supported by careful historical and clinical analysis, pointing to a disease entity which he termed acute interstitial pancreatitis. He felt able "to justify the conclusion that they were dealing with a type of acute pancreatitis with edema, swelling or induration which was distinct from the usual cases of acute pancreatitis in showing no evidence of gland necrosis, hemorrhage or suppuration." His description of the macroscopic, microscopic and clinical pictures probably warrants a separation of this type of acute pancreatitis into a class by itself. Although certain authors have claimed otherwise, Elman stated that this entity is "not merely an early stage in the development of frank pancreatic necrosis." Even if Elman's interpretation is wrong, there is good reason to believe that this pathologic cycle, which subsides prematurely, produces an independent clinical picture. The first group of cases described in this paper were of this type.

The second group of cases described here is differentiated from the first by a much more severe reaction, with necrosis, hemorrhage and even suppuration of the pancreas. This condition has found considerable space in the surgical literature and as a result has become rather familiar, although acute pancreatic necrosis is not a common malady. Another term used almost interchangeably with acute pancreatic necrosis is acute hemorrhagic pancreatitis, for necrosis and hemorrhage frequently go hand in hand.

Symptomatology—Fitz,¹ in 1889, made the statement

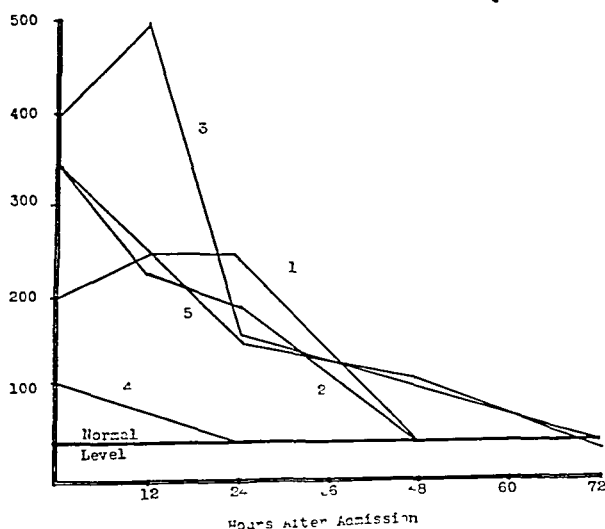
Acute pancreatitis is to be suspected when a previously healthy person, or sufferer from occasional attacks of indigestion, is suddenly seized with violent

³ Elman, R. Acute Interstitial Pancreatitis, Surg., Gynec. & Obst. 57:291-309 (Sept.) 1933.

pain in the epigastrium followed by vomiting and collapse, and, in the course of twenty-four hours, by a circumscribed epigastric swelling tympanitic or resistant, with a slight rise in temperature

He was, of course, reterring to the condition called acute pancreatic necrosis

The symptoms of acute interstitial pancreatitis, although similar to those of acute pancreatic necrosis, are not fulminating and do not produce shock and circulatory collapse but have a tendency to subside in a few hours or days. A point of interest in this series is the history of previous, though milder, attacks in the cases of interstitial pancreatitis



Curves representing the amylase content of the blood in 5 cases of acute interstitial pancreatitis. The patient in case 4 entered the hospital with a subsiding attack which had begun one week previously. The relatively low curve is probably due to this fact.

Summary of Important Observations in Two Groups of Cases of Acute Pancreatitis Treated Without Operation

Case	Acute Interstitial Pancreatitis					Acute Pancreatic Necrosis				
	1	2	3	4	5	6	7	8	9	10
Age	42	60	60	60	27	61	51	33	24	42
Sex	M	F	M	M	F	M	F	F	M	M
Previous attacks	Yes	Yes	Yes	Yes	Yes	No	No	?	No	No
Epigastric pain and vomiting	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prostration (severe)	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes
High value for blood amylase	Yes	Yes	Yes	Yes	Yes	Yes	?	?	?	No
Leukocytosis	Yes	No	No	Yes	Yes	No	Yes	Yes	No	Yes
Blood sugar mg /100 cc	114	122	100	100	153	90	?	2 -	140	215
Jaundice	No	No	Yes	Yes	No	Yes	?	?	Yes	Yes
Termination	Recovery	Recovery	Recovery	Recovery	Recovery	Death	Death	Death	Death	Death

The outstanding and constant symptom of acute pancreatitis, regardless of type, is the severity of the pain. One has only to review a few authentic case histories and observe the frequency of a misdiagnosis of perforated peptic ulcer to realize the type and intensity of pain. The location is not constant, and this has been a source of confusion. Although the patient usually points to the epigastrium as the site of disturbance, he may also direct attention to either the right or the left upper quadrant of the abdomen, or he may complain of generalized abdominal pain. Radiation of pain is also described, either straight through from the epigastrium to the interscapular region or to the small of the back. Nausea and repeated vomiting are the rule.

Careful palpation will frequently disclose an area of tenderness in the epigastrium and the left side of the hypochondrium, over the region of the pancreas. Elman stated "In a few cases I was able to outline a Head-zone of skin hyperesthesia along the left costal margin"⁴. Often, however, the tenderness may be diffuse over the entire upper part of the abdomen, which may sometimes be distended and tympanitic to percussion, with the "silence" of peritonitis. This finding is easily explained by stimulation of the celiac and superior mesenteric ganglions and plexuses, which lie close to the pancreas. Distention probably explains the occasional misdiagnosis of intestinal obstruction.

In cases of acute pancreatic necrosis there is generally definite evidence of collapse, frequently accompanied by cyanosis. This condition gives all of the picture produced by shock, such as a fall in blood pressure, rapid, weak and thready pulse, cold and clammy skin and apprehension on the part of the patient. De Klimko⁵ described his cases in three groups, according to the clinical picture. The first group includes those with a sudden onset and rapid progress with death in a short time, autopsy showing extensive fat necrosis and pancreatic necrosis. In the second group the symptoms are less severe and tend to subside. The last group comprises the cases of mild involvement. Obviously, in a great portion of the second and third groups the disease would fit in with the type described in this report as acute interstitial pancreatitis.

Many patients show frank jaundice, others have an icteric scleral tinge. This is probably explained by the course of the common duct through the head of the pancreas, where it may readily be compressed in a case of pancreatic edema or tumor. There is usually mild leukocytosis, the increased leukocyte count being scarcely significant the first day but rising to 15,000 or 20,000 on the second day. The erythrocytes

⁴ Elman, R. The Diagnosis and Treatment of Acute Pancreatitis, *Am J Digest Dis & Nutrition* 4 732-736 (Jan) 1938

⁵ de Klimko, D. Surgical Treatment of Acute Pancreatitis, *Surg Gynec & Obst* 63 89-95 (July) 1936

show little change. The urine may occasionally contain sugar during the acute phase of the attack and at times may contain urobilinogen.

The cornerstone in the diagnosis of acute pancreatitis lies in the determination of the value for diastase (amylase) in the blood. Much has been written on the biochemistry of blood diastase and much more remains to be made clear. There is not complete agreement as to its source or function (Clasen, Johnstone and Orr⁶). Elman, Arneson and Graham⁷ reported observations in the human being which led them to believe that a low value for blood amylase meant destruction of the acinar tissues of the pancreas whereas increased amylase in the blood resulted from obstruction of the ducts. This would explain how early in the disease there may be a high value for blood amylase, followed later, if there is considerable pancreatic necrosis, by a low value. In interstitial pancreatitis also a high level occurs early, but the progressive fall, usually in a day or two, has a different significance, being closely correlated with the subsiding symptoms. Somogyi⁸ has correlated low values for blood diastase with severe hepatic injury.

The sugar tolerance curve has been used by de Klimko⁵ as an aid in diagnosis. He asserted that for patients with subsiding acute pancreatitis the curve shows higher values during the first thirty minutes and does not fall to the normal for some time. He called attention also to an elevation of the serum lipase in this condition, which he attributed to the fat necrosis associated with acute pancreatitis. It is of interest to note the elevation of the cholesterol content of the blood in many of the cases of acute pancreatitis.

Differential Diagnosis—Acute cholecystitis or biliary colic, perforated duodenal or gastric ulcers, intestinal obstruction and acute coronary thrombosis are the diseases which usually present a problem in the differential diagnosis of acute pancreatitis. The diagnostic error lies not so much in the lack of a thorough work-up as in the failure to consider acute pancreatitis as a possibility in every case of disease of the upper part of the abdomen. In case of doubt in diagnosis the diastase content of the blood should always be determined. In a series of 18 cases of acute pancreatitis, in all of which the characteristic curves for blood amylase were obtained, Elman³ showed that in 9, or 50 per cent, the diagnosis on admission was biliary colic or acute cholecystitis. In cases of the interstitial type of acute pancreatitis as in cases of chronic

6 Clasen, A. C., Johnstone, P. N. and Orr, T. G. Blood Amylase in Experimental Pancreatitis, *Surg. Gynec. & Obst.* 59: 756-761 (Nov.) 1934.

7 Elman, R., Arneson, N. and Graham, E. A. Value of Blood Amylase Estimations in Diagnosis of Pancreatic Disease. *Clinical Study Arch. Surg.* 19: 943-967 (Dec., pt. 1) 1929.

8 Somogyi, cited in footnote 2.

cholecystitis, there is frequently a history of previous attacks with absence of symptoms during the interval. Every case of supposed biliary colic should be studied with pancreatitis in mind, there will frequently be a high value for blood diastase. A perforated peptic ulcer will give in most cases a typical and diagnostic clinical picture. The suddenness of onset and the location and character of the pain may be reproduced by acute pancreatitis. However, a past history of ulcer, the presence of abdominal rigidity and especially roentgenograms showing air under the diaphragm are all diagnostic aids. It must be kept in mind that an ulcer on the posterior surface of the stomach may rupture into the lesser peritoneal cavity and evoke an elevation of the amylase content of the blood as a result of direct irritation of the pancreas as by the contents of the stomach (Probstein, Gray and Wheeler⁹).

Acute intestinal obstruction when high and accompanied (as it is) by frequent vomiting will sometimes rather closely simulate acute pancreatitis. However, the peristaltic rushes, the roentgen pictures, the fluctuating character of the pain and the presence of a cause should dispel any confusion.

Etiology—The older literature has so frequently been cited that it will not be detailed here. A recent review is that of Robins¹⁰. This author, as have others, notably Opie,¹¹ emphasized the entrance of bile into the pancreatic ducts as the most frequent cause. In 1921, Archibald¹² discussed this phase of the disease and stated the conviction that the regurgitation of bile into the pancreatic system is the usual causative factor. Three years later, Eggers¹³ advanced his hypothesis that the lesion in acute pancreatitis is due to the release of pancreatic juices into the adjoining tissues, and he added that infection in itself has little to contribute to the pathologic picture. In 1933, Finney¹⁴ summed up the matter by stating that there is activation within the gland of pancreatic ferments by a reflux of bile, causing a chemical necrosis in which infection plays a secondary part. Important in this connection is the experimental transplantation of living pancreatic tissue into a window of

9 Probstein, J. G., Gray, S., and Wheeler, P. A. Blood Diastase in Acutely Perforating Peptic Ulcers, *Proc. Soc. Exper. Biol. & Med.* **37** 613-615 (Jan) 1938.

10 Robins, C. Bile Tract and Acute Pancreatitis, *Ann. Surg.* **103** 875-885 (June) 1936.

11 Opie, E. L. Disease of the Pancreas. Its Cause and Nature, ed. 2, Philadelphia, J. B. Lippincott Company, 1910, pp. 15 and 200.

12 Archibald, E. Further Data Concerning the Experimental Production of Pancreatitis, *Ann. Surg.* **74** 426-433 (Oct.) 1921.

13 Eggers, C. Acute Pancreatitis, *Ann. Surg.* **80** 193-209 (Aug.) 1924.

14 Finney, J. M. Pancreatic Emergencies, *Ann. Surg.* **98** 750-759 (Oct.) 1933.

the duodenum, as accomplished by Dragstedt¹⁵. This produced no digestion, whereas when the pancreas was implanted into the gallbladder there was necrosis of the pancreatic tissues exposed to the bile. There are two possibilities in the hydrodynamics of the retrojection of bile into the pancreatic duct system: first, mechanical obstruction due to an impacted stone and second, spasm of the sphincter of Oddi. The latter is anatomically possible in at least 20 per cent of all adults, according to pathologic and anatomic studies. Autopsies and examination of the common duct during operative procedures have shown sufficient evidence to place this factor on a definite etiologic basis. The benefit of cholecystectomy as a therapeutic measure is said to be in the fact that after this procedure there is dilatation of the common duct and of the sphincter of Oddi. That there is a close relation between disorders of the biliary system and acute pancreatitis is a matter of agreement in the minds of most authors who have discussed this subject. Statistics¹⁶ reveal the rather convincing fact that as many as 70 per cent of patients with acute pancreatitis have associated disease of the gallbladder.

It has recently been demonstrated that in certain cases the administration of amyl nitrite relieves the severe pain of acute pancreatitis, probably by relaxing the sphincter of Oddi. Amadon¹⁷ reported a case of acute pancreatitis in which during operation agenesis of the gallbladder was revealed. This observation was regarded by the author as significant in that it indicated a disturbance in the pressure balance normally present in the biliary system, which permitted a regurgitation of bile into the pancreatic duct. Pavel,¹⁸ in discussing jaundice caused by spasm of the sphincter of Oddi, stated that it is difficult to appreciate the exact nature and location of the lesions giving rise to this reflex spasm. He added that inflammation in the gallbladder, common bile duct, pancreas and duodenum may initiate a spastic condition of the sphincter.

A contrasting view of the etiology of acute pancreatic necrosis is that of Rich,¹⁹ who minimized the role of bile and presented evidence that metaplasia of the epithelium of the ducts may play an important role.

Death from acute pancreatitis is due to toxemia resulting from absorption of necrotic glandular elements. The toxicity of these sub-

15 Dragstedt, L. R., Hammond, H. E., and Ellis, J. C. Pathogenesis of Acute Pancreatitis (Acute Pancreatic Necrosis). *Arch Surg* **28** 232-291 (Feb.) 1934.

16 Schmieden, V., and Sebening, W. Chirurgie des Pankreas. *Arch f klin Chir* **148** 319, 1927.

17 Amadon, P. Agenesis of the Gall Bladder Associated with Pancreatitis. *Am J Surg* **19** 263-267 (Feb.) 1933.

18 Pavel, I. Jaundice Caused by Functional Obstruction. *J A M A* **110** 566-569 (Feb 19) 1938.

19 Rich, A. R., and Duff, G. L. Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis. *Bull Johns Hopkin Hosp* **58** 212-259 (March) 1936.

stances has been demonstrated by the use of cross circulation in dogs, however, further experimental procedures have shown that the toxicity is dependent on bacterial action. Organisms in healthy pancreatic and hepatic tissues either resemble or are identical with *Clostridium welchii*.

In considering the etiology of acute interstitial pancreatitis in contrast to that of acute pancreatic necrosis, one observes that the actual trigger mechanism "touching off" the episode is probably somewhat different in the two types though the blocking of the duct system is the fundamental genetic basis of both. The blocking is temporary and recurrent in the former, tending to increase in severity, whereas in the latter there is a more permanent obstruction, resulting in the more dramatic climax. Perhaps in a large proportion of cases of the transient condition there is a functional spasm of the sphincter of Oddi, and in the necrotic type there is a more permanent mechanical obstruction secondary to cholelithiasis or some similar condition.

Pathology—Data with regard to the pathologic changes observed in acute interstitial pancreatitis are limited, because it is exceptional for this lesion to be seen at the autopsy table. Most of the gross findings have been recorded from direct observations during a laparotomy, and most of the microscopic descriptions have been made possible by removal of tissue for biopsy during operation. As early as 1898, Korte²⁰ described several patients with acute symptoms referable to the upper part of the abdomen in whom surgical exploration was done and in whom the only abnormality found was edema of the pancreas. Later, others, both in Europe and in America discussed these conditions, so frequently confused with intestinal obstruction and other abdominal emergencies, in an effort to clarify the issue. Elman³ reviewed the literature, added his own observations and proposed recognition of an entity which he termed acute interstitial pancreatitis. In this condition the gland appears tense and almost glistening as though engorged with fluids, and on palpation this sensation of tension is confirmed by a peculiar hardness, almost akin to the "woody" character of malignant tumor. Examination will explain the relative ease with which the glandular portion of the common bile duct might be compressed in the process. It should be emphasized that these changes may not be observed if the patient is operated on after acute symptoms have subsided. There may be fat necrosis limited to the peripancreatic tissues without actual pancreatic necrosis. Further exploration of the biliary system will in many cases reveal some disease, usually chronic cholecystitis or cholelithiasis. Microscopically one finds a gland which is fairly intact in marked contrast to the cellular holocaust observed in pancreatic

²⁰ Korte, W. Die chirurgischen Krankheiten und die Verletzungen des Pankreas, Stuttgart, Ferdinand Enke, 1898, p. 175.

necrosis The acini remain structurally distinct, and the inflammatory nature of the disease is seen in the leukocytic invasion of the interacinar and interlobular tissues The infiltration is confined in great part to the framework of the pancreas though frequently there are inflammatory cells and debris within the ducts Polymorphs are the predominating cells involved This pathologic process is to be differentiated from chronic pancreatitis, in which fibrosis of the interacinar tissues plays the predominant role, though some pathologists consider the latter change to be sequential to the former

Acute pancreatic necrosis is truly an exact and descriptive term, as any surgeon who has inspected and palpated the pancreas in such a condition will agree The gland may lose all semblance of its normal anatomic structure and stand out as a necrotic mass surrounded to a greater or lesser degree by adjacent viscera in an attempt at walling off the process In contrast to the interstitial type, the pancreas is soft, dark red, purplish or even black, depending on the pathologic stage There are varying degrees of fat necrosis which is scattered widely over the pancreas or the surrounding omentum and mesentery On opening the peritoneal cavity the surgeon is confronted with free brownish fluid, formed by increased peritoneal transudation This fluid is often mixed with particles of necrotic material

Under the microscope these sections of necrosis are distinctive in their utter lack of structure The acini are destroyed and about the areas are zones of polymorphic infiltration According to Gatewood,²¹ this *infiltration and swelling of the gland are responsible for the severity of the pain produced* Little more than this can be stated about the histopathologic picture of this condition

Therapy—There is no necessity for any type of immediate surgical intervention in cases of acute interstitial pancreatitis, the patients therefore, fall into the group which may be safely watched The therapy is symptomatic until the acute symptoms subside at which time one may resort to prophylactic surgical intervention in an effort to prevent recurrence As the biliary system appears to be the most frequent offender, most surgical procedures consist of cholecystectomy, provided of course, that there is cholecystographic evidence of a pathologic gallbladder At operation the common duct may be explored (often via the cystic duct) and drainage of bile through the cystic duct carried out In conjunction with exploration of the common duct probes may be passed into the duodenum actively dilating the sphincter

Symptomatic therapy during the acute phase of acute interstitial pancreatitis consists in the administration of carbohydrates either by

21 Gatewood Acute and Chronic Pancreatitis S Clin North America 17 473-487 (April) 1937

mouth or parenterally in sufficient quantities to protect the liver, which is so often involved. Sedation plays an important role in the comfort of the patient and may even prevent secondary attacks brought about by nervousness and apprehension. Amyl nitrite has been suggested recently to relieve spasm of the sphincter of Oddi. Morphine is of little value and may actually increase the intensity of the pain or precipitate another attack.

About the therapy of acute pancreatic necrosis there is much controversy. Finney²¹ prescribed early laparotomy and drainage as the method of choice. On the other hand, Smead²² questioned the wisdom of early operation with wide exposure, incision and tamponade of the pancreas and drainage of the biliary system, favoring a delay of several days or even a week or two.

There are also extreme differences in the reported mortality of acute pancreatic necrosis. Although in most statistics the rate ranges around 50 per cent or higher, Mikkelsen²³ between the years 1926 and 1934 treated 30 patients with acute pancreatitis with a mortality rate of only 7.5 per cent. He expressed opposition to early surgical intervention. De Klinkó,⁵ to whose series of cases I have already referred, agreed that after immediate operation there was a mortality rate of 90 per cent, whereas after delayed operation the rate fell to 12 per cent. While statistics such as these may seem convincing, they must be analyzed and only patients with true pancreatic necrosis considered. Unless this is done, mortality statistics are valueless, because they include instances of acute interstitial pancreatitis, which it is now known will subside spontaneously.

It appears from the literature thus briefly cited that the consensus bears out the belief that early surgical intervention in cases of acute pancreatic necrosis is not advisable and that operation should be delayed. That indefinite delay is not the proper course, however, is indicated by the present series, in which such a policy resulted in the death of all 5 patients.

SUMMARY

Ten cases of acute pancreatitis are reported, segregated for further analysis into two groups of 5 cases each. Investigation reveals differences which are significant if the condition called acute pancreatic necrosis is to be recognized, it is in cases of this condition that conservative therapy must be replaced by other treatment, notably laparotomy, with a view to reducing the exceedingly high mortality. In this series

²² Smead, L. Treatment of Acute Pancreatic Necrosis, *Am J Surg* 32: 487-497 (June) 1936.

²³ Mikkelsen, O. Pancreatitis acuta. Schwere Fälle, besonders im Hinblick ihrer konservativen Behandlung, *Acta chir Scandinav* 75: 373-415, 1934.

all patients with this condition died after conservative therapy. Operation for drainage of the lesser peritoneal cavity has long been the accepted procedure and is based on the favorable effect of allowing active trypsin an exit, thus minimizing its destructive action on the pancreatic and surrounding tissues. Preparatory measures, such as transfusions and administration of fluids, must be used in view of the shock which is so frequently present. Doubtless the mortality of this disease will always be high, but on the basis of this report a change from conservative therapy is indicated. A reasonable procedure would seem to be treatment by conservative measures during a preparatory period followed by operation as soon as possible. Patients suffering from the transient type of interstitial pancreatitis recover promptly, the symptoms of those harboring a necrotic pancreas do not automatically subside. Patients can be converted into better risks during the period of observation, this will reduce the high mortality of laparotomy.

CONCLUSION

Five patients with acute interstitial pancreatitis were treated conservatively, and all recovered, 5 patients with acute pancreatic necrosis were similarly treated, and all died. Both types of disease can be diagnosed by early determination of the value for blood amylase. The clinical differential diagnosis of the two conditions is discussed, this is important in order to reduce the mortality of the second condition, acute pancreatic necrosis. It is suggested that in cases of the latter entity operation be carried out as soon as the diagnosis is made provided the patient can be made operable by appropriate preparatory procedures.

EFFECT OF SCLEROSING SUBSTANCES ON HEALING OF FRACTURES

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It is not within the scope of this paper to discuss the causes of delayed union or nonunion of fractures. It may be briefly mentioned that local as well as constitutional factors come into consideration and that in spite of careful attention to these conditions frequently no union can be obtained. The field for an efficient stimulant of regeneration of bone is open.

While the humoral theory of osseous growth finds numerous proponents, another school of thought is gaining popularity, this school teaches that bone is formed by direct action of specific cells. Although the problem is still awaiting solution, the cellular theory is supported by the results of many experiments and by many clinical observations. It is possible, therefore, that a stimulant of osseous growth which can be used in selected cases of nonunion or delayed union may be found. Such an agent must fulfil the following conditions: (1) It must not cause any injurious local effects or a systemic reaction, (2) it must be sterile, and (3) its injection must be followed by a painless therapeutic response.

Our attention has been attracted to the use of sclerosing solutions in the treatment of hernia. The rationale of this procedure has been firmly established, since it has been shown that the solutions used for injection cause a proliferation of tissues, which gradually closes the hernial ring. The therapeutic effectiveness of injection of sclerosing substances in selected cases of hernia induced Schultz¹ to employ it in treatment of subluxation of the temporomandibular joint. This use of the procedure was successful.

Bone is modified connective tissue, wherever and whenever bone is formed, the process starts with undifferentiated mesoblastic cells and culminates in transformation of the mesodermal tissue into the bone.

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1 Schultz, L. W. Treatment for Subluxation of the Temporomandibular Joint, J. A. M. A. **109** 1032 (Sept 25) 1937

under the influence of local or systemic stimuli. The following experiments were undertaken with the hope that injection of sclerosing substances would stimulate regeneration of bone.

EXPERIMENTAL METHOD

Three substances were selected for the experiments: proliferol 'B', proliferol 'T' and sylvasol.²

In 24 rats under ether anesthesia fractures were produced manually in the center of the right tibia. Two days later 0.125 cc of proliferol 'B' was injected at the site of fracture in 6 rats. 6 animals received a double dose of the same solution. 6 rats were given injections of 0.125 cc of physiologic solution of sodium chloride, and 0.25 cc of the same saline solution was injected into each of the remaining 6 rats. The injections were repeated every second day to a total of twelve. One animal of each group was killed eight, twenty-one, twenty-eight, forty and seventy days after the first injection. Roentgenograms of the fractured extremity were taken immediately after the animal had been killed; the extremity was then carefully dissected and placed in solution of formaldehyde U. S. P. for microscopic studies. After decalcification of the bone serial sections were made longitudinally through the site of fracture.

In a series of identical experiments proliferol 'T' was used, and in the third series sylvasol was used.

RESULTS

The first roentgenograms, taken ten days after the production of the fracture, or eight days after the first injection, showed that all fractures were produced in practically the same portion of the tibia. The second series of pictures, taken twenty-three days after the production of the fracture or twenty-one days after the first injection, showed beginning callus formation; the position of the fragments was not, of course, identical in all the animals. The third series of pictures, taken thirty days after the production of the fracture or twenty-eight days after the first injection, showed more advanced callus formation, with resulting increase in the density of the shadows. The last series of pictures was taken seventy-two days after the production of the fracture or seventy days after the first injection. Firm consolidation of the fragments was

2 According to the manufacturer proliferol 'B' is a distillate of several botanic drugs of known proliferating properties containing thymol and 0.5 per cent tannic acid. Proliferol 'T' is a mixture of 7 parts of proliferol 'B' and 1 part of thuja injection fluid. (Thuja injection fluid or thuja mixture consists of 50 parts phenol, 25 parts alcohol and 25 parts Lloyd's specific tincture of thuja.)

Sylvasol, formerly known as sylvasol, is a 5 per cent solution of the sodium salts of certain of the fatty acids of the oil extracted from a seed of the willow group.

These preparations have not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

Proliferol 'B' and proliferol 'T' were supplied by the Ulmer Pharmaceutical Company, Minneapolis. Sylvasol, by G. D. Searle & Co., Chicago.

revealed. A comparison of the pictures belonging to the same series at no time disclosed any differences between the fractures treated with proliferol "B," those treated with proliferol "T," those treated with sylvasol, those treated with saline solution as far as the time of the



A, photomicrograph ($\times 94$) of a section of a rat's leg twenty-one days after production of a fracture of the tibia followed by injections of saline solution. The tissue at the left of the specimen is bone, that on the right, muscular tissue. There is no evidence of an inflammatory reaction. *B*, photomicrograph ($\times 94$) of a section of a rat's leg twenty-one days after production of a fracture of the tibia followed by injections of proliferol T. The tissue at the left of the specimen is bone, that on the right, muscular tissue. Numerous fibroblasts are scattered between the muscular fibers.

first appearance of the callus, the density of the shadows or the ultimate consolidation of the fragments was concerned

As can be seen in the photomicrographs, twenty-one days after the first injection there were no signs of an inflammatory exudate after injection of proliferol 'T', in comparison with the fracture treated with injections of saline solution however there was a marked increase of fibroblasts around the bone and between the bundles of muscles. Similar findings were made in the fractures treated with proliferol 'B' and in those treated with slynasol. No considerable differences could be detected in the effect of the three sclerosing substances except that the amount of newly formed connective tissue seemed to be larger around fractures treated with proliferol 'T' than around those treated with the other two sclerosing substances. Histologic studies of specimens obtained at longer intervals after the first injection showed increase and condensation of the fibrous tissue in the soft parts at the site of fracture.

A study of sections made at various times after the first injection failed to demonstrate any differences in the size of the callus in the animals treated with injections of saline solution and in those treated with sclerosing substances.

COMMENT

It cannot be stated definitely that the sclerosing substances used in the experiments just described do or do not stimulate callus formation, because various sources of error must be considered. One of them lies in the technic of preparation of sections. It is obviously impossible to make comparable sections at the site of fracture in the different animals used for experiment and the deviations of direction will naturally be responsible for a spurious increase of the size of the callus. Another cause of the apparent failure to stimulate callus formation may be attributed to mechanical factors. After the first two injections the induration of the soft tissues surrounding the fracture made impossible the introduction of the sclerosing solution between the fragments, so that the injected fluid was probably deposited at some distance from the fracture and could not reach its destination.

Although neither the roentgenologic nor the histologic findings could demonstrate stimulation of the callus by injections of the sclerosing solutions, one effect was undoubtedly obtained, that is formation of new, dense connective tissue around the fracture. This histologic change was responsible for the clinical observation of a rock-hard induration. Such change may offer a certain advantage, serving as "internal splinting" of the fragments. Theoretically a disadvantage could be created by the formation of very dense tissue with resulting compression of the blood vessels and impairment of blood supply to the site of the

fracture This, however, was not the case, for the number and size of the capillaries in specimens obtained from fractures treated with sclerosing solutions compared favorably with the number and size of those observed in the control specimens

SUMMARY

Injections of 0.125 and 0.25 cc of proliferol "B," proliferol "T" or sylnasol at the site of fracture of the tibia in rats failed to produce roentgenologically or histologically demonstrable stimulation of regeneration of bone

No untoward local or general effects were observed

Marked fibrosis followed injections of the sclerosing substances

CONCLUSION

Although injection of sclerosing substances at the site of fractures of the tibia in rats apparently did not stimulate the rate of regeneration or the amount of the newly formed bone, the resulting fibrosis of the surrounding tissues may have a therapeutic value in selected cases, serving as an internal splint for the bone fragments

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Dr Otto F Kampmeier, head of the Department of Anatomy, and Dr George E Wakerlin, head of the Department of Physiology, made helpful suggestions and criticisms concerning this work

SUNRAY HEMANGIOMA OF THE SKULL

REPORT OF A CASE

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Hemangioma of the skull is exceedingly rare. A recent thorough review of the literature by Anspach¹ disclosed a total of 21 reported cases. He added a detailed account of a case of his own, emphasizing the special roentgen features. The tumor was first diagnosed as a sarcoma. An operation was attempted but had to be abandoned because of profuse bleeding. However, after fifteen years the patient was still in good health and roentgenograms of the skull showed the characteristic "sunburst" effect of a benign slowly growing hemangioma.

It is of interest that in 7 of the 21 cases of hemangioma of the skull operation was performed. Brief reference to them follows. In 1877 Ehrmann² performed trephination of the skull of a 40 year old woman who had been suffering from severe headaches for many years. She died of meningitis shortly thereafter. At autopsy a soft cavernous hemangioma was seen in the left parietal region, involving the diploë but leaving the inner and outer tables of the skull intact. Zajaczkowski³ in 1901, removed a cavernous angioma from the left parietal region of a 38 year old patient who had been aware of the growth for six years. The tumor pulsated synchronously with the heart and was attached to the dura. In 1905, von Bergmann⁴ removed a myelogenous hemangioma from the occipital bone by joining three trephine holes which were well outside the limits of the tumor. The tumor measured 3 by 4 by 1 cm and did not involve the dura.

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1 Anspach W E. Sunray Hemangioma of Bone with Special Reference to Roentgen Signs, *J A M A* **108** 617 (Feb 20) 1937

2 Ehrmann 1847 cited by Schone G. Ueber einen Fall von myelogenem Hämangiom des Os occipitale. *Beitr z path Anat u z allg Path* 1905 supp 7 p 685

3 Zajaczkowski, A. Ein Fall von Angioma cavernosum des Stirnbeines. *abstracted Centralbl f Chir* **28** 507 1901

4 von Bergmann cited by Schone G. Ueber einen Fall von myelogenem Hämangiom des Os occipitale. *Beitr z path Anat u z allg Path* 1905 supp 7 p 685

Complete removal of a hemangioma of the skull was reported by Cushing.⁵ The tumor was regarded as a melanotic sarcoma until three years after the operation, when the specimen was again studied and the final diagnosis of cavernous hemangioma made.

Dikansky⁶ reported 2 cases of cavernous hemangioma of the skull in which recovery followed operation. One of the patients had intractable headaches, vomiting and convulsions associated with unconsciousness. Bucy and Capp⁷ have clearly demonstrated that "sunburst" trabeculations are characteristic features of the roentgen picture of hemangioma in a flat bone. However, we find no report of a correct diagnosis prior to the successful removal of such a tumor from the skull. In the case to be described a hemangioma of the skull was diagnosed preoperatively.

REPORT OF A CASE

History—On Aug 3, 1937, a 47 year old white woman, a housewife, was admitted to the hospital because of a growth in the left parietal region. Her health was otherwise excellent, and her past medical history had no relation to the present complaint. She recalled that on a number of occasions in the past few years she had bumped her head against a closet projecting above the kitchen sink, usually striking the site of the present lesion. She had first become aware of the tumor six months before admission. Since that time there had been a gradual increase in the size of the growth. There was no pain or discomfort except for a dull ache when pressure was applied to the tumor. The patient sought hospitalization because she was greatly concerned about the possible malignant character of the growth and the danger that it might lead to cerebral involvement.

Examination—The patient was well nourished and well developed. She was ambulatory and was not in acute distress. Over the left parietal region was a hard, bony protuberance about 3 cm. in diameter, which seemed to merge into the bones of the skull. Firm pressure in the region of the protuberance caused a vague feeling of discomfort, but there was no local tenderness, pulsation or bruit. The blood pressure was 95 systolic and 65 diastolic. Physical examination otherwise revealed nothing abnormal. Roentgen examination of the skull showed an irregular area of rarefaction in the left parietal region, about 3 cm. in diameter, involving chiefly the outer table of bone. The structure of this area (fig 1) suggested trabeculations of bone radiating from a common center and had the appearance of a "sunburst" hemangioma.

Course—The patient was advised that the tumor was benign and self limited. Nevertheless, she remained intensely agitated and feared that possibly the physicians concealed information as to the true nature of the growth. When she became increasingly disturbed emotionally, so that she could not eat or sleep, an operation was thought to be indicated.

5 Cushing, H. Surgical End-Results in General, with a Case of Cavernous Hemangioma of the Skull in Particular, *Surg, Gynec & Obst* **36** 303, 1923.

6 Dikansky, M. Zwei Falle von Haemangioma cavernosum des Schädels. *Deutsche Ztschr f Chir* **236** 648, 1932.

7 Bucy, P. C., and Capp, C. S. Primary Hemangioma of Bone, with Special Reference to Roentgenologic Diagnosis, *Am J Roentgenol* **23** 1, 1930.

Operation (Dr Abraham Kaplan) —On August 6, with the patient under the influence of avertin with amylene hydrate and with the use of local anesthesia induced with procaine hydrochloride, a vertical incision was made over the tumor. As the skin and the galea were retracted, the periosteum over the growth was found completely intact (fig 2). Four burr holes were made about 1 inch (2.5 cm) from the periphery of the vascular tumor. The burr holes were then joined with

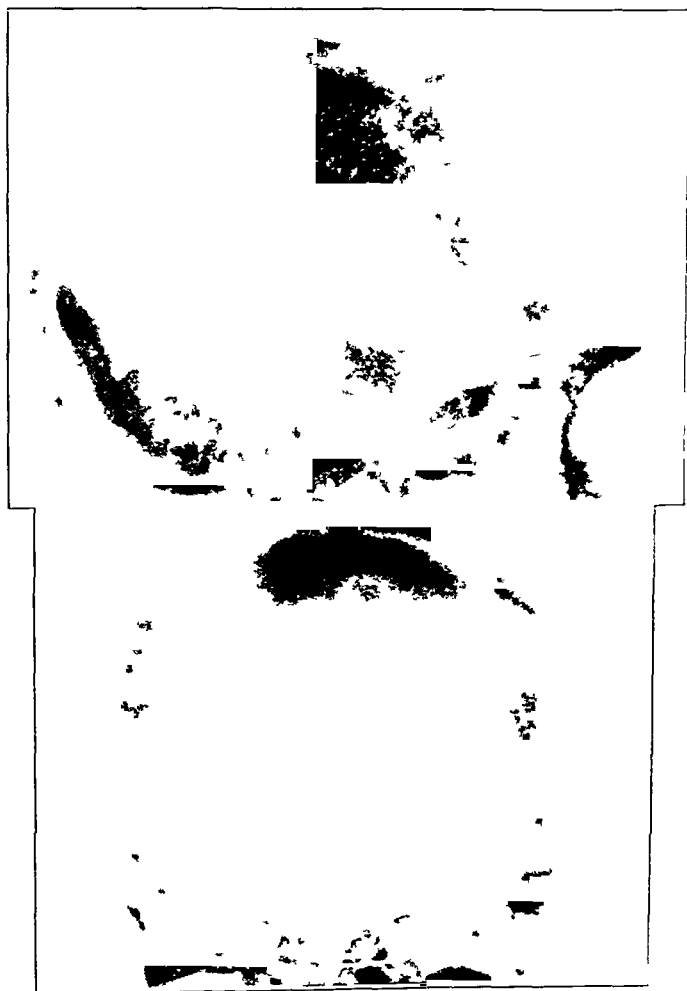


Fig 1—Roentgenograms of the skull showing the characteristic trabeculations of bone radiating from a common center

a Gigli saw, and the attendant bleeding was controlled with bone wax. As the tumor was elevated, it separated easily from the dura. No sooner was the tumor removed than the troublesome bleeding ceased. The dura was not involved. The pulse and blood pressure remained at a good level and transfusion was not necessary. Closure of the muscle, galea and skin over the resulting defect afforded natural and secure protection.



Fig 2—Outer surface of the tumor, with intact periosteum



Fig 3—Inner surface of the specimen. The periphery shows normal thickness of the skull, the central portion presents an ovoid mottled area of thickening with fine granular nodulations.

Pathologic Report—Gross Examination The specimen consisted of a resected portion of the skull measuring 5 by 4.5 by 2 cm (fig 3). The periphery of the resected bone was of normal thickness and appearance. The central portion of the specimen presented an ovoid area of thickening measuring 3.5 by 3.5 by 2 cm, the surfaces of which were mottled blue and yellow with fine granular nodulations. The tumor mass was well demarcated on the surface, and on section the inner and outer tables were seen to be thinned but intact. Throughout the mass were coarse bony trabeculations which radiated outward from the center.

Microscopic Examination (fig 4) The bone marrow was completely replaced by fatty angiomatous tissue which surrounded many thin bony trabeculae. The

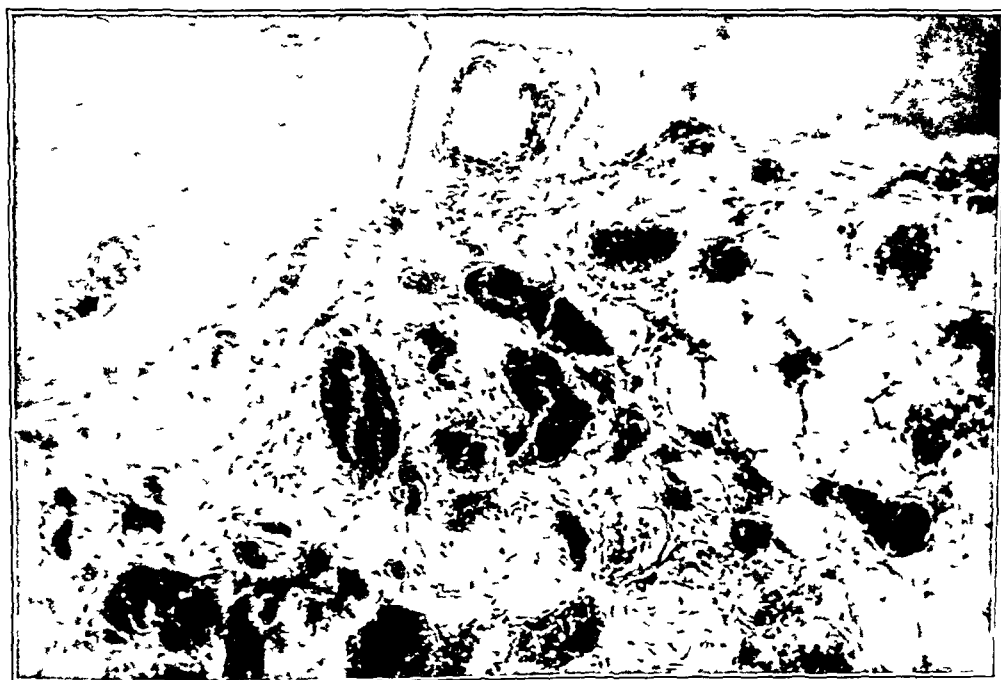


Fig 4—Microscopic section of the tumor showing the intact periosteum and the fatty angiomatous tissue surrounded by many thin bony trabeculae.

periosteum was intact. The stroma consisted of delicate strands of connective tissue accompanied by slender bony trabeculae. There was no evidence of mitosis.

Diagnosis—A diagnosis of hemangioma was made.

Postoperative Course—Recovery was uneventful and the patient was discharged from the hospital on the eighth postoperative day. At the time of writing one and one-half years after discharge she is entirely well physically and mentally.

COMMENT

This case illustrates many of the typical features of hemangioma of the skull. Reported mild local trauma over the site of the tumor is so frequently found in the histories of patients with this lesion that there

appears to be a definite etiologic relation. Although the rate of growth of such a tumor may be slow, it eventually becomes so large and so vascular that operative intervention is hazardous. The subjective complaints, though insignificant at first, steadily increase with the growth of the neoplasm. Headaches become more frequent and may be associated with vomiting or even with convulsions and unconsciousness.

Histologic studies show that a hemangioma grows slowly in the diploe of the skull, arising from a center and radiating toward the inner and outer tables. As growth continues, trabeculations are formed in the bone, which give the characteristic "sunburst" appearance in the roentgenogram. The cortex of the bone may be destroyed, but the periosteum remains intact. The tumor may undergo cystic degeneration and begin to pulsate, at which time even a slight trauma may be followed by serious complications. Most often such a tumor has been thought clinically to be sarcoma. There is some congenital disposition to such growth,⁸ and it may be associated with hemangiomas in other organs.⁹

Increasing familiarity with the characteristic roentgen picture of sunray hemangioma makes it probable that the correct diagnosis will be made earlier and with greater frequency. The mental and physical symptoms as well as the cosmetic effects resulting from this usually benign tumor may make operative intervention advisable. Although roentgen therapy may be used as an alternative procedure, Bucy and Capp⁷ have found that excision of the hemangioma usually provides the earliest and best results. If excision is done outside the border of the tumor and the surgeon is prepared to control the troublesome bleeding, there should be little difficulty or risk in removing the growth.

SUMMARY

A case of sunray hemangioma of the skull is presented. This rare type of tumor can now be diagnosed preoperatively. The typical clinical roentgen and therapeutic features are discussed, and the surgical aspect is briefly reviewed.

⁸ Toynbee, J. An Account of Two Vascular Tumors Developed in the Substance of Bone, *Lancet* **2** 676, 1845, Aneurism by Anastomosis in the Substance of the Parietal Bones, *ibid* **1** 230, 1847.

⁹ Major, R. H., and Black, D. R. A Huge Hemangioma of the Liver Associated with Hemangioma of the Skull and Cystic Adrenals, *Am J M Sc* **156** 469, 1918.

SULFAPYRIDINE IN TREATMENT OF PNEUMONIA, WITH SPECIAL REFERENCE TO POST- OPERATIVE PNEUMONIA

H CORWIN HINSHAW, M D, PH D

AND

HERMAN J MOERSCH, M D

ROCHESTER, MINN

No report has come to our attention concerning the effect of sultapyridine (2-[paraaminobenzenesulfonamido]-pyridine) on postoperative pneumonia. We wish to record our experience with this drug in 21 cases of postoperative pneumonia and 6 cases of primary pneumonia. This includes the cases of all patients with uncomplicated pneumonia under our personal supervision to whom we have given the drug up to the time of writing this report.

DOSE

Patients usually were given 15 grains (1 Gm.) of sultapyridine by mouth every four hours day and night (90 grains, or 6 Gm., per day). The first dose, and sometimes the second dose also, was doubled, making a total of either 105 or 120 grains (7 or 8 Gm.) during the first twenty-four hours. The duration of treatment is indicated in the charts.

UNFAVORABLE EFFECTS

No seriously bad results could be attributed to treatment with sultapyridine. Significant leukopenia was not observed. Marked cyanosis was not encountered, and there were no cases of hemolytic anemia, drug rash, drug fever or other serious complications.

Approximately half (15) of the patients treated complained of nausea. About half (8) of these 15 were troubled with vomiting sufficiently severe to persuade us to shorten the contemplated course of treatment. In no instance was it necessary to deny the patient needed treatment because of vomiting. Trouble was lessened when the drug was given with milk or other food. Severe nausea was minimized by inhalation of pure oxygen through a nasal mask for one to two hours after each dose. It must be emphasized to the patient, the nurse and the physician that the occurrence of nausea is not justification for discontinuing the use of this drug when it is really needed. Nausea does not indicate a serious toxic response; it is merely an uncomfortable reaction.

From the Division of Medicine, the Mayo Clinic

THERAPEUTIC RESULTS

The temperature charts (figs 1 to 8) demonstrate the results. Each dot represents the maximal temperature on one day. The maximal temperature of nearly half of the patients approached normal within twenty-four hours after the beginning of treatment with sulfapyridine. The condition of most of the remainder was significantly improved in

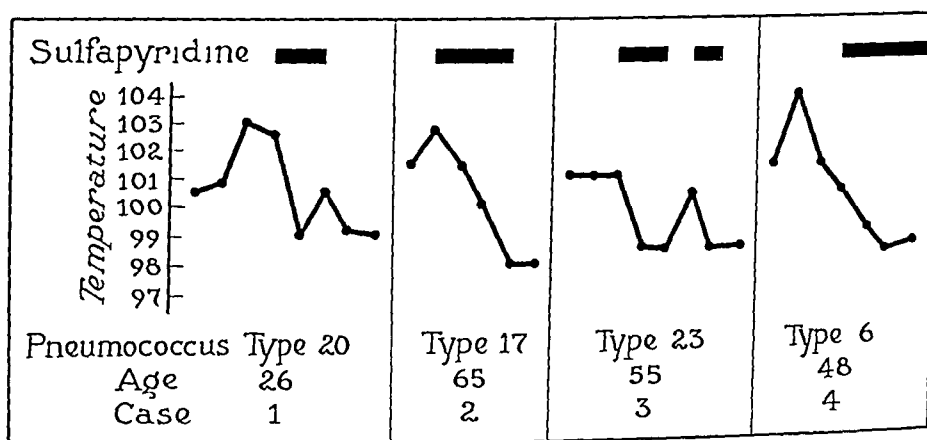


Fig 1—Postoperative pneumococcal pneumonia treated with sulfapyridine. In this and in all the following charts each dot represents the maximal temperature for one day. Note the interrupted treatment in case 3 and its relation to fever.

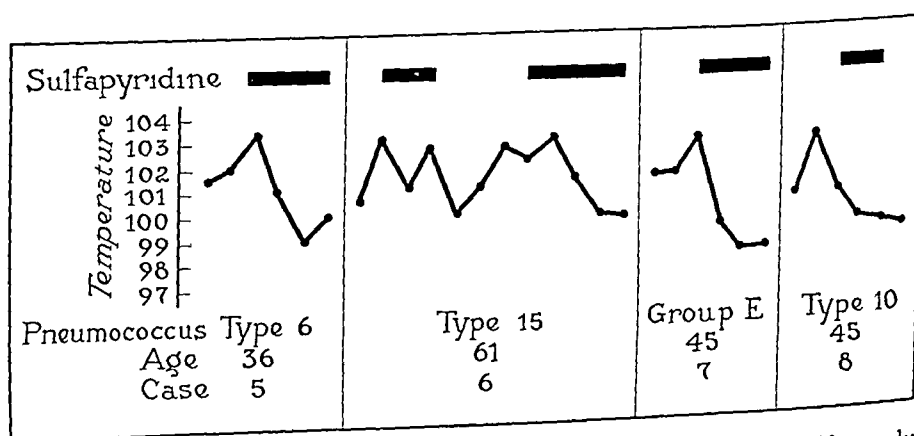


Fig 2—Postoperative pneumococcal pneumonia treated with sulfapyridine. Treatment was interrupted in case 6 after secondary closure of the wound, coughing had caused extrusion of viscera. The fever was due in part to localized peritonitis.

forty-eight to seventy-two hours. The results were similar whether or not pneumococci were found in the sputum. Postoperative pneumonia responded as well as primary pneumonia. Older patients responded as well as younger ones. Only 1 death occurred. This was in a case of early fulminating postoperative pneumonia which developed on the

second day after extraperitoneal resection of a carcinoma of the colon (case 12). The patient first received sulfanilamide (total dose 100 grains or 6.5 Gm) and rabbit serum (100,000 units, type 13) on the second day of the pneumonia. Administration of sulfapyridine was started thirty hours before death and the patient received 135 grains

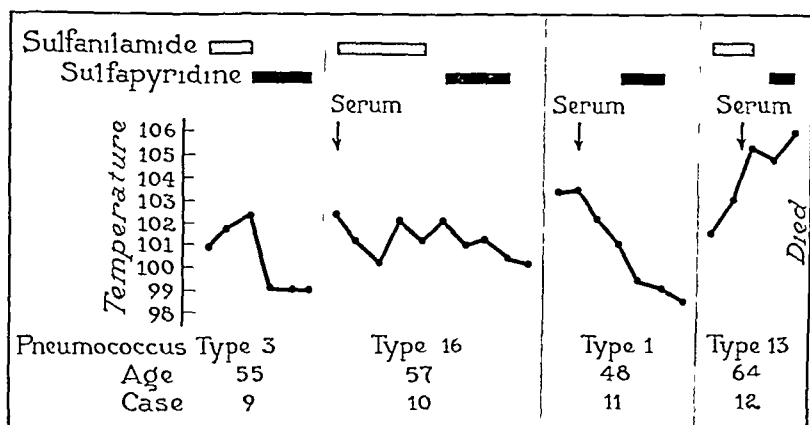


Fig 3—Postoperative pneumococcal pneumonia. In each case more than one form of treatment was employed. In cases 10, 11, and 12, 100,000 units each of appropriate antipneumococcus serum was given. Note the apparent effectiveness of sulfapyridine after the apparent failure of sulfanilamide. A roentgenogram taken in case 11 is shown in figure 9a.

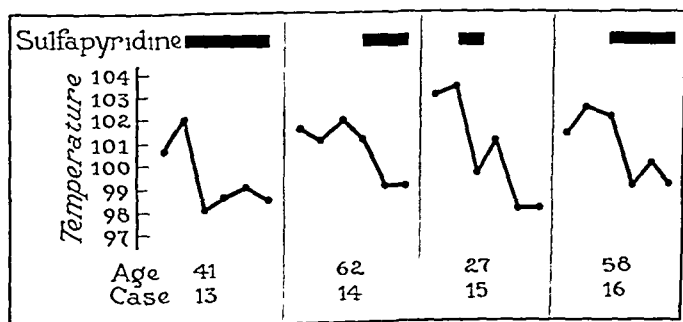


Fig 4—Postoperative pneumonia treated with sulfapyridine. Pneumococci were not found in the sputum. A roentgenogram taken in case 13 is shown in figure 9b.

(9 Gm). As the patient was comatose the drug was given by duodenal tube. Necropsy disclosed extensive bilateral pneumonia.

In cases 3, 6, and 21, treatment was interrupted. Close correlation between administration of sulfapyridine and reduction of fever was apparent. In case 9, sulfanilamide and sulfapyridine were given at differ-

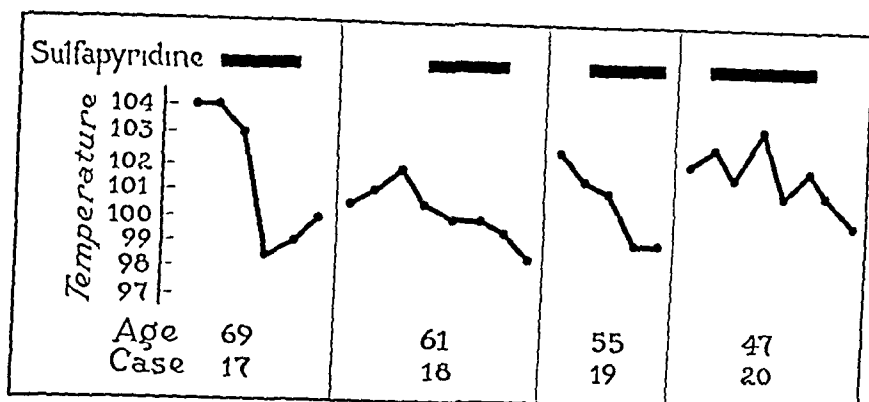


Fig 5—Postoperative pneumonia treated with sulfapyridine. Pneumococci were not found in the sputum. Pneumonia was demonstrated roentgenographically in case 20 when treatment was started. Although fever continued for three or four days, evidences of pneumonia, including roentgenographic signs, were absent four days later when treatment was stopped.

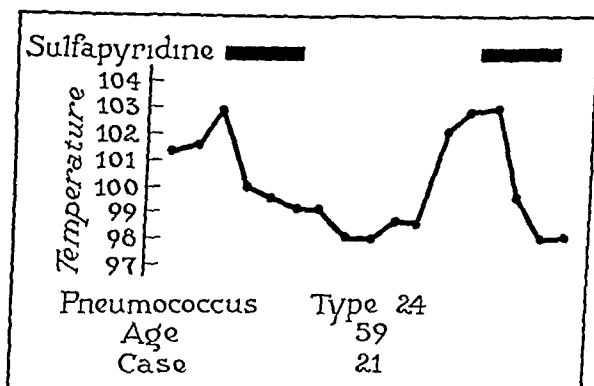


Fig 6—Postoperative pneumococcic pneumonia, treated with sulfapyridine. The first course of treatment was for pneumonia of the lower lobe of the right lung (pneumococcus type 24). One week later pneumonia developed in the lower lobe of the left lung, with no pneumococci in the sputum. The response to treatment in both instances was excellent.

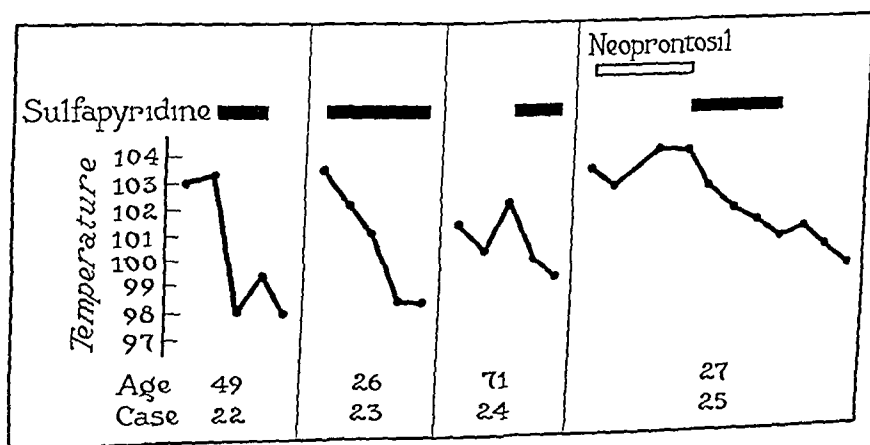


Fig 7—Primary pneumonia treated with sulfapyridine. Pneumococci were not found in the sputum. Note that in case 25 sulfapyridine seemed to be beneficial after neoprontosil apparently had failed.

ent times and an apparent difference between the effectiveness of the drugs was noted. In cases 25 and 26 neoprontosil (administered orally) and sulfapyridine were given, with results similar to those obtained in case 9. In cases 10 and 12 antipneumococcus serum (100,000 units

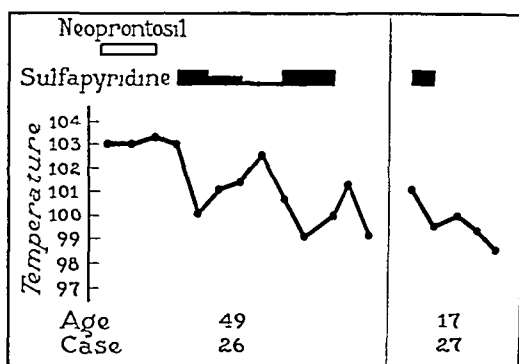


Fig 8—Primary pneumonia treated with sulfapyridine. Note that in case 26 reduction of the dose resulted in recurrence of fever but that the fever subsided when administration of the full dose was resumed. Note the apparent failure of neoprontosil.

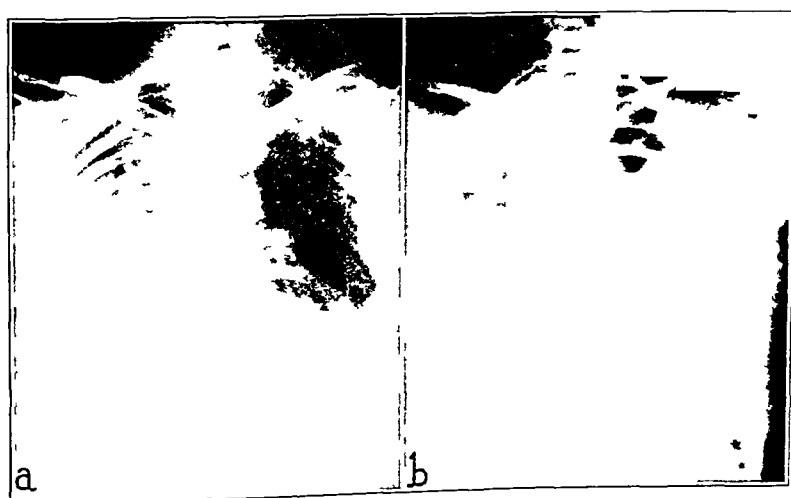


Fig 9—Thoracic roentgenogram (a) in case 11 and (b) in case 13.

in each case), sulfanilamide and sulfapyridine were administered. In case 11 the response to serum therapy (100,000 units) was prompt but because some degree of fever persisted treatment with sulfapyridine was instituted forty-eight hours after serum therapy had been begun. It must be emphasized that other patients whose cases are not reported here responded satisfactorily to serum, sulfanilamide or neoprontosil.

and therefore did not receive sulfapyridine. Certain of the charts merely demonstrate that some patients who did not respond to other treatment did subsequently respond to sulfapyridine.

The diagnosis of pneumonia was confirmed by roentgen examination in every case. The roentgenograms taken in 2 of the cases (cases 11 and 13) are shown in figure 9. In cases of mild involvement treatment with sulfapyridine usually was denied if early spontaneous improvement could be anticipated. Sulfapyridine usually was withheld until evidence of serious progressive pneumonia had been obtained. Most patients received nonspecific supportive treatment, including oxygen therapy, hyperventilation with carbon dioxide, intravenous administration of fluids and similar measures. Three patients received positive pressure therapy for pulmonary edema, with successful results. At least half of the patients in the series were so seriously ill that recovery would have been doubtful without sulfapyridine or specific therapy.

COMMENT

Surgeons will welcome this evidence that postoperative pneumonia frequently is arrested by administration of sulfapyridine.

Efforts to avoid atelectasis and aspiration may prevent, or even abort, very early postoperative pneumonia. If these measures are ineffectual, however, within a day or two the problem becomes one of overcoming an acute pulmonary infection. The organisms responsible for such an infection frequently are pneumococci. Of the 21 cases of postoperative pneumonia, pneumococci appeared to be the causative organisms in 13. Several types were identified, including type I. The organisms were recognized by the Neufeld method of typing sputum.

Sulfapyridine cannot be administered parenterally because of its insolubility. The drug is not available, therefore, to patients who are not permitted oral medication after a surgical operation. This constitutes a distinct disadvantage.

Optimal concentrations of sulfapyridine in the blood are not known. Maximal concentrations of the drug varied from 29 to 77 mg per hundred cubic centimeters in our cases. Between these limits no significant difference in therapeutic or toxic effects was noted.

Successful administration of the drug may depend on adherence to several rules. 1 Nausea is not an indication for discontinuing administration of the drug. 2 Frequent administration preferably every four hours day and night seems desirable. 3 Favorable response should be shown in twenty-four to forty-eight hours by a sharp decline in fever. 4 Prolonged administration is not usually necessary and may be dangerous.

The prognosis of pneumonia is often dependent on the age of the patient. Most therapeutic measures diminish in efficacy as age increases.

Available information appears to indicate that administration of sultapyridine may be an exception to this rule. More than half of our patients with postoperative pneumonia were 55 years of age or more. Only 4 patients were less than 45 years of age. The age of each patient is recorded on the charts.

SUMMARY

Sultapyridine may promptly arrest the progress of postoperative as well as primary pneumonia. It may be successful when other chemotherapeutic agents apparently have failed. It is effective in the treatment of elderly as well as the young patients. Pneumococci are frequently the predominant organisms in the sputum of patients with postoperative pneumonia. The drug appears to be equally effective when pneumococci are not identified in the sputum.

Dr. D. F. Robertson, Associate Medical Director, Merck & Co., Rahway, N. J., supplied the sultapyridine used in this study.

CHANGING EXPERIENCES WITH BENIGN AND MALIGNANT LESIONS OF THE COLON AND OF THE RECTUM

L. CLARENCE COHN, M.D.

BALTIMORE

During the first sixteen years of my experience as an associate of Dr. Bloodgood, I took part in the diagnostic study and operation in 276 cases of lesions of the colon and of the rectum. In addition, I studied sections and roentgenograms in 125 cases of similar lesions treated elsewhere, in which material was sent to the clinic for diagnosis. Table I summarizes these experiences.

In 136 of the 276 personally observed cases, approximately 50 per cent, and in 72 of the 125 cases in which we were sent material, approximately 60 per cent, cancer was present. In the former group, in the great majority of instances the cancer had reached the stage in which one could make the diagnosis by digital palpation and by inspection through a proctoscope when the rectum was involved or by study of a roentgenogram taken after a barium sulfate enema when the lesion was situated higher. Consequently, biopsy was seldom performed. For cancer of the colon (exclusive of the cecum) and for cancer of the rectum, appendicostomy or cecostomy has usually been the first treatment. In the cases of operable cancer the involved segment of bowel was later excised in one or two stages, usually with restoration of the continuity of the colon when the lesion was proximal to the lower portion of the sigmoid and usually with permanent colostomy when the cancer involved the rectum or the rectosigmoid junction.

Roentgen therapy alone or before or after operation was used in 12 of the 49 cases of cancer of the colon and in 27 of the 86 cases of cancer of the rectum, and there is no evidence that it prolonged life, although there is no question that it added materially to the comfort of the patient in a number of instances. In 2 cases of cancer involving the lower part of the rectum the treatment was with radium and roentgen rays. Later I shall refer to these 2 cases in connection with 2 recent cases of cancer of the lower part of the rectum so treated.

The lesion was in the colon in approximately 36 per cent and in the rectum in approximately 64 per cent of the group of 140 patients with benign lesions of the colon and rectum examined in the clinic. Or

the 53 cases in which material was sent to the clinic for diagnosis the colon was involved in approximately 43 per cent and the rectum in approximately 57 per cent (table 1)

Congenital malformations, ptosis postoperative adhesions, amebic dysentery, colitis and tuberculosis accounted for the great majority of benign lesions of the colon, and in 42 of the 50 instances in which the patients were under our own observation there was no operation. In 4

TABLE 1—*Lesions of the Colon and of the Rectum (1919 to 1935)*

Lesions clinically observed	276 (colon 100 rectum 176)
Cancer	136 (colon 80 rectum 56)
Benign lesions	140 (colon 20 rectum 120)
Lesions observed from tissue sections and roentgenograms	125 (colon 59 rectum 66)
Cancer	72 (colon 36 rectum 36)
Benign lesions	53 (colon 23 rectum 30)

* In 8 cases these lesions were treated by operation. Acute obstruction from volvulus was present in 3 mesenteric thrombosis in 1 perforation in 1 and a fecal fistula in the cecum in 1. In 42 cases no operation was done. The conditions were congenital malformations ptosis postoperative adhesions amebic dysentery and colitis.

† In 9 cases a polyp was present. In the remaining 81 cases there were miscellaneous conditions (fissure and fistula in ano ischiorectal abscess pilonidal sinus prolapse of the rectum or proctitis).

‡ In 2 cases the condition was obstruction due to volvulus in 2 a polyp was present and in 19 there were various chronic inflammatory lesions including colitis and pericolicitis ptosis and tuberculosis.

§ In 12 cases a polyp was present in the other 18 there were miscellaneous conditions.

TABLE 2—*Lesions of the Colon and of the Rectum (Oct 21 1935 to May 21 1938)*

Lesions clinically observed	56 (colon 19 rectum 37)
Cancer	16 (colon 10 rectum 6)
Benign lesions	40 (colon 9 rectum 31)
Lesions studied from tissue sections and roentgenograms	7 (colon 3 rectum 4)
Cancer	4 (colon 1 rectum 3)
Benign lesions	3 (colon 2 rectum 1)

* In 5 cases these lesions were treated by operation. Acute obstruction due to volvulus was present in 2 polyp of the sigmoid in 2 and diverticulitis of the transverse colon in 1. In 4 cases no operation was done. Simple colitis was observed in 1 of these ulcerative colitis in 2 and ptosis in 2.

† In 1 of these cases the condition was lymphogranuloma venereum in the remaining 30 miscellaneous conditions were present (hemorrhoid fistula ischiorectal abscess pilonidal sinus or fissure).

* Tuberculosis was present in 1 case and a chronic inflammatory lesion in 1.

of the 8 surgically treated patients with benign lesions of the colon there was acute obstruction from volvulus or mesenteric thrombosis. In only 2 instances a case of benign polyp of the sigmoid and a case of diverticulitis of the sigmoid, was cancer considered in the preoperative diagnosis.

A large miscellaneous group of the commoner lesions of the rectum composed the majority of benign lesions of the rectum, and benign polypoid tumors visible through the proctoscope accounted for the large minority.

Table 2 is a summary of the experience of my colleague Dr George A Stewart and myself with lesions of the colon and rectum in the past two

and one-half years. It is this changing experience that has stimulated me to review our material and to report in abstract 8 recent cases. Cases 1, 2 and 3 are cases of benign lesions of the colon, in cases 1 and 2 there were precancerous lesions of the sigmoid flexure, and in case 3 there were diverticulitis of the transverse colon and multiple diverticulosis of the sigmoid. Cases 4, 5, 6, 7 and 8 are cases of lesions of the rectum. In case 4 the condition was venereal lymphogranuloma, and in cases 5, 6, 7 and 8 it was early operable carcinoma of the lower third of the rectum. This condition was treated by roentgen and radium therapy.

REPORT OF CASES

CASE 1—H. M. B., a white man aged 46, consulted me Aug. 13, 1936 because he had noticed bright red blood in the stools. He stated that his father had died of cancer of the sigmoid which on exploration had been found inoperable. The patient had first noticed the presence of bright red blood in the stools on two or three occasions about one year before he sought our advice, and again, temporarily, seven months later. So far as he knew, there had been no recurrence until three weeks before he came to the clinic. The quantity of blood at this time was much greater than on previous occasions and with the blood there was considerable mucus. On four or five occasions during the past three weeks there had been a normal stool, followed in a few minutes by a desire to evacuate the bowel again. The feces of the second evacuation contained a large quantity of mucus streaked with blood. During the previous three weeks there had been a number of attacks of diarrhea, four or five watery stools being passed in twenty-four hours, followed the next day by a normal evacuation of the bowel.

During the preceding two weeks there had been two independent studies by other physicians. These studies included in each instance a proctoscopic examination. In 1 instance a complete gastrointestinal fluoroscopic and roentgen study had been done, in the other, a roentgenogram of the colon had been taken after a barium sulfate enema. The results were reported to be entirely negative. I repeated the proctoscopic examination on two occasions, with negative results. At St. Agnes' Hospital Drs. E. B. Freeman and E. L. Flippin and I noted in the fluoroscopic examination of the colon during a barium sulfate enema a slight irregularity in the distal portion of the sigmoid. A roentgenogram taken immediately afterward showed no filling defect, but the sigmoid loop was distinctly displaced from its usual position, suggesting to us the presence of adhesions (fig. 1).

On August 15, 16 and 17 I inspected the stools and on each occasion found fresh blood in considerable quantity.

On August 19 I performed appendicostomy and on August 28 resection of the sigmoid portion of the colon, followed by a lateral anastomosis by the Bloodgood method (fig. 2).

The operative findings consisted of adhesions between the lower part of the middle third of the sigmoid and the omentum, and just at this point there was a distinctly palpable, freely movable polypoid tumor about 2 cm. in diameter, which was not visible through the wall of the bowel. I was unable to palpate any other polypi in the colon between the rectosigmoid junction and the splenic flexure. Photographs of the gross specimen (fig. 3) and photomicrographs (fig. 4) show the structure of the tumor.



Fig 1—Roentgenogram of the colon after a barium sulfate enema in case 1. Note the dislocation of the sigmoid loop as described in the text. A benign adenomatous polyp was found at the junction of the lower and the middle third of the sigmoid loop.

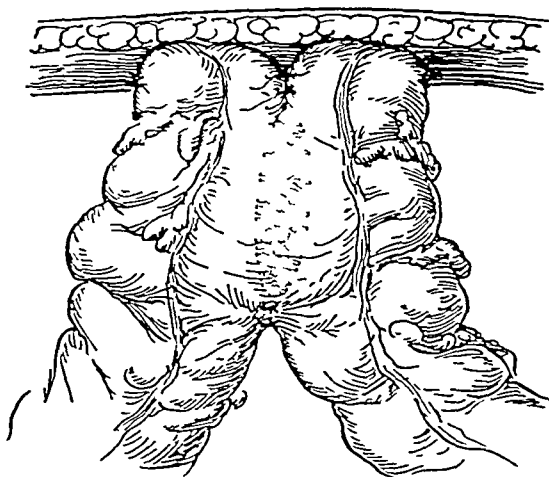


Fig 2—Drawing illustrating Bloodgood's method of lateral anastomosis of the colon (from Alexis McGlennan in Lewis D. Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc. 1930, vol 7, chap 4, p 105).

On the eighth postoperative day there was a leak to the outside at the site of the anastomosis, and the fistula was still present on the patient's discharge from the hospital, on October 5. In fact, it was not healed until Jan 18, 1937, three and one-half months later. The appendicostomy wound healed of its own accord, although there was occasional intermittent discharge of cecal contents for some months.

CASE 2—W. B., a white man aged 47, the brother of the patient in case 1, consulted me on Jan 26, 1937 because of bright red blood and mucus in the stools for three months. There was slight tenderness in the region of the sigmoid on

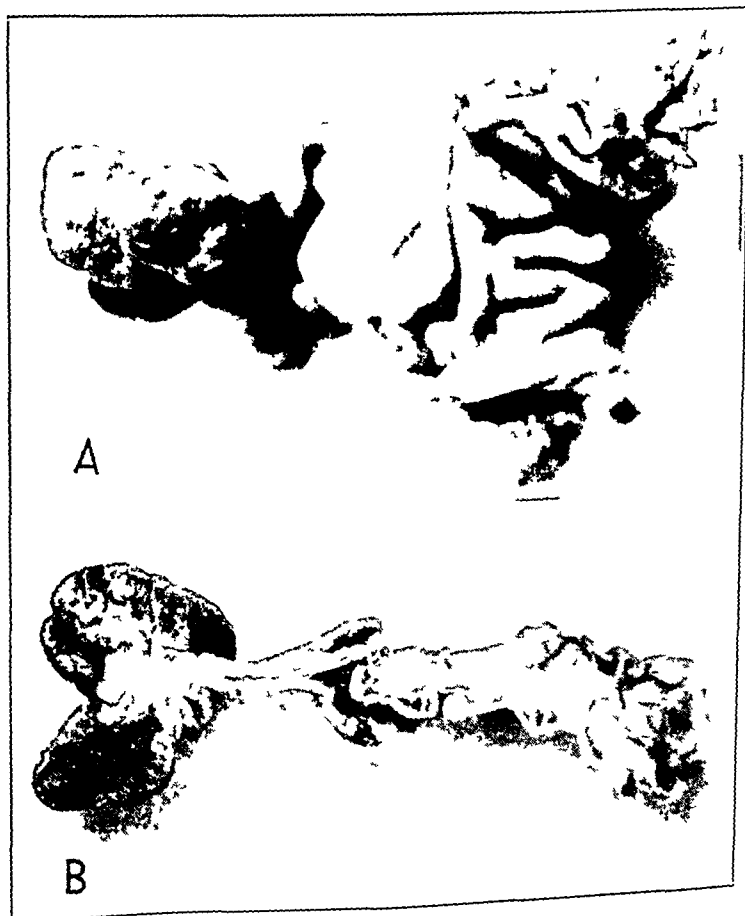


Fig 3—Photographs of the gross specimen in case 1, showing the polypoid tumor and the resected segment of the sigmoid.

abdominal palpation. No lesion was present throughout the 24 cm of the bowel visible through the proctoscope, but mucus and blood were seen running down from the bowel above. A roentgenogram of the colon taken after a barium enema was entirely normal (fig 5). Six months more elapsed before the patient consented to an operation, notwithstanding the constant presence of blood and mucus in the stools.

On July 9 I resected the sigmoid portion of the colon and made a lateral anastomosis by the Bloodgood method (fig 2). The operative findings consisted of a freely movable and nonadherent sigmoid containing a palpable polyp approximately 2 cm in diameter. The polyp was located near the summit of the sigmoid loop. No other polypi were palpable between the rectosigmoid junction and the

splenic flexure. Photographs of the gross specimen (fig 6) and photomicrographs (fig 7) show the structure of the tumor.

The operative wound healed per primam intentionem, and the patient left the hospital on July 26, seventeen days after the operation. He returned on August



Fig 4—*A*, medium low power photomicrograph of the tumor in case 1 showing the adenomatous character of the growth. *B*, high power photomicrograph of the tumor in case 1. Compare the clear cells with small nuclei on the right with the cells containing the hyperchromatic nuclei on the left.

15, twenty days later, because of a small draining sinus in the middle of the scar. This was entirely healed on September 24.

Comment—The similarity in age, symptoms, duration of bleeding, location, size and gross and microscopic appearance of the lesions in these two brothers was striking. The difference in the appearance of the roentgenograms is accounted for by the presence of adhesions in the first case. The hereditary factor in polyposis intestini has been well established by the studies of Dukes. I am not familiar with any comparable

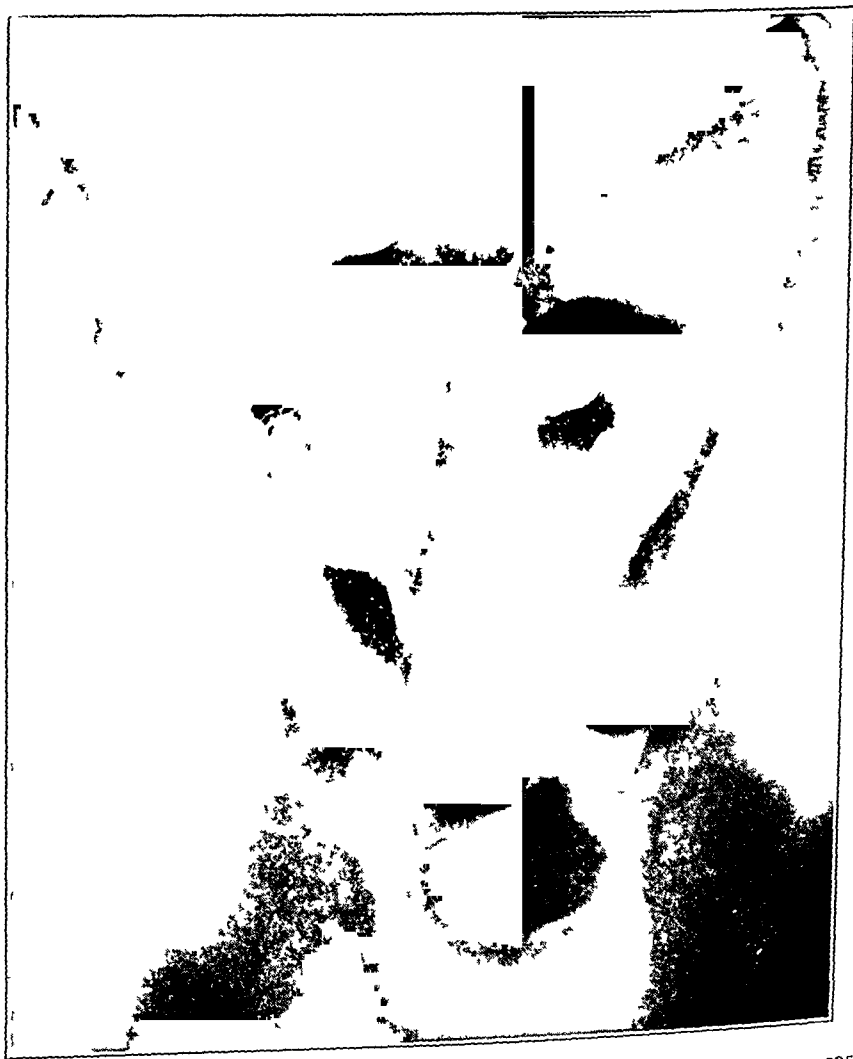


Fig 5—Roentgenogram of the colon after a barium sulfate enema in case 2. The sigmoid loop occupies its normal position. A benign adenomatous polyp was found near the summit of the loop.

studies on solitary polypus of the colon, but it seems that the relation between the sigmoid carcinoma in the father and the presence of a polypoid adenoma of the sigmoid in 2 sons is more than casual. The 2 cases demonstrate the advisability of laparotomy when blood and mucus are constantly present in the stools even when careful proctoscopic and roentgen examinations fail to reveal the site of the lesion. At operation

search should be made for multiple tumors in the colon. Histologically these tumors are true adenomas and show changes in morphologic and staining characteristics which are definitely precancerous, therefore even



Fig. 6—Photographs of the gross specimen in case 2, showing the polypoid tumor and the resected segment of the sigmoid

though they are pedunculated I prefer resection and anastomosis to simple excision. When there are adhesions to the wall of the bowel at the site of the tumor as in case 1 resection seems almost imperative. Perhaps it is unnecessary to make a preliminary appendicostomy as

was done in the first case. The advantage of the Bloodgood method is that both ends of the colon can be sutured extraperitoneally between the fasciae, so that if a leak occurs the infection will find its way to the surface more readily.

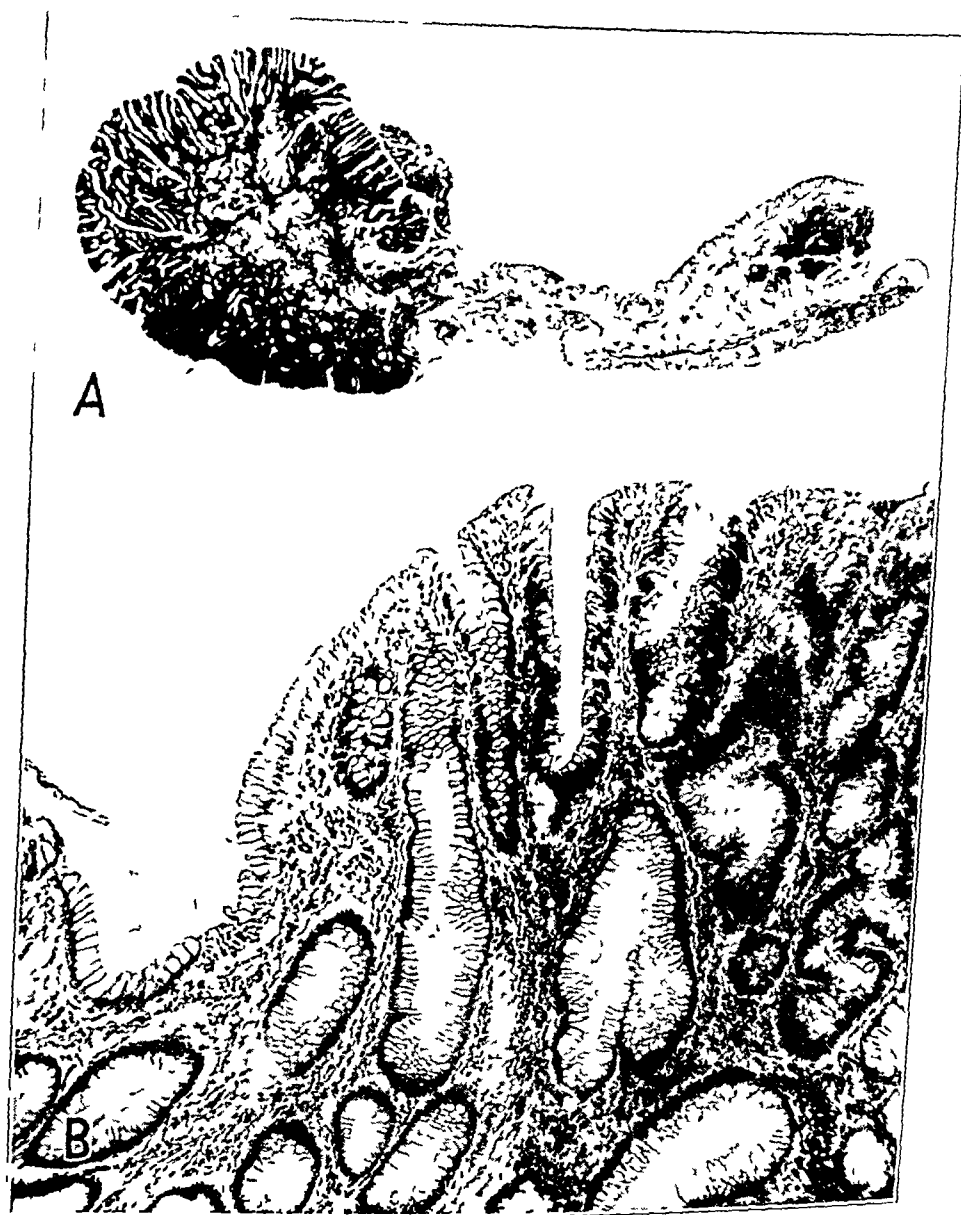


Fig 7—A, low power photomicrograph of the tumor in case 2, showing the polyp and the pedicle. B, medium low power photomicrograph of the same tumor, showing the polyp and the pedicle. Note the adenomatous character of the growth. Contrast the clear cells with small nuclei at the bases on the left with the hyperchromatic nuclei on the right.

CASE 3—R. M., a white man aged 59, consulted us on Dec 20, 1932 because of pain in the midzone of the abdomen of one month's duration, associated with increasing constipation. Fourteen months previously a calculus had been removed.

from the right kidney, and twenty-five years previously appendectomy had been performed

A roentgenogram of the colon taken after a barium sulfate enema showed multiple diverticula in the sigmoid and a single, larger diverticulum in the right portion of the transverse colon. The symptoms disappeared quickly under treatment with liquid petrolatum and a mild laxative. Roentgenograms of the colon taken at yearly intervals showed no changes in the diverticula during the years 1933, 1934 and 1935 (fig 8 A). When the patient returned for examination on Feb 11, 1937 after a year in Europe, he complained of severe colic across the upper part of the abdomen of ten days' duration. Palpation elicited tenderness 3 inches (7.5 cm) to the right of the umbilicus and also below the old appendectomy scar. A roentgenogram of the colon showed a distinct filling defect at the site of the old diverticulum in the right side of the transverse colon (fig 8 B). There were no changes in the diverticula in the sigmoid.



Fig 8—A, roentgenogram of the colon after a barium sulfate enema in case 3. This picture was taken Dec 6 1935. There is a single diverticulum in the right side of the transverse colon and there are multiple smaller diverticula in the sigmoid. B, roentgenogram of the colon after a barium sulfate enema in case 3. This picture was taken Feb 11 1937, fourteen months after the picture shown in figure 8. There is a distinct filling defect in the right side of the transverse colon at the site of the diverticulum shown in figure 8.

At operation, on February 20 I found a large fatty omentum densely adherent in the right lower quadrant to the cecum and to the parietal peritoneum probably the result of the old appendicitis. The right two thirds of the transverse colon was dislocated downward and at the site of the diverticulum the colon was bound by adhesions to the mesentery of the duodenum. A narrow band of adhesions surrounded the colon at this point and constricted the lumen. The diverticulum was encased in a mass of indurated fat containing calcified nodules.

Exposure of the right half of the transverse colon was obtained by division of the omentum and liberation of the adherent loop by excision of a portion of the

peritoneum of the mesentery of the duodenum together with the indurated fat surrounding the diverticulum. This allowed the colon to resume its normal position, and the division of the band of adhesions encircling the colon at the site of the stricture permitted it to resume its normal shape. The diverticulum was then excised and the stump ligated and inverted (fig 9 A).

On the third day after operation acute parotitis developed on the left side, which rapidly cleared up under roentgen therapy. The abdominal wound healed per primam intentionem and the patient left the hospital on the thirtieth day after the operation.

When he returned from a trip abroad, on November 15, he complained of occasional abdominal cramps, and examination revealed a small postoperative hernia. The symptoms disappeared in a few weeks under medical treatment, and



Fig 9—*A*, photograph of the bisected gross specimen in case 3, showing (above) the mucosa of the diverticulum and (below) the enveloping mass of indurated fat. *B*, roentgenogram of the colon after a barium sulfate enema in case 3. This picture was taken Nov 15, 1937, nine months after the operation.

the hernia was controlled by an elastic belt. Figure 9 *B* is a roentgenogram of the colon taken November 15, nine months after the operation.

Comment—In this case the roentgenogram showing the deformed colon and the filling defect at the site of the preexisting diverticulum indicated diverticulitis rather than carcinoma. However, in a recent case I observed carcinoma at the rectosigmoid junction coexisting with multiple diverticula in the sigmoid, and others have made similar observations. Deforming adhesions may occur in conjunction with diverticulitis, benign and malignant tumors and other conditions, and in the

absence of earlier roentgenograms the preoperative diagnosis may be difficult to establish.

CASE 4—W. R., a white man aged 47, was admitted to the surgical service of St. Agnes' Hospital through the outpatient department on June 25, 1938. For three months he had noticed diarrhea, tenesmus, and the presence of blood and pus in the stools. Examination revealed a distended abdomen. The anus admitted only the tip of the gloved finger. No enlarged lymphatic nodes were palpable.



Fig. 10—Roentgenogram of the colon after a barium sulfate enema in case 4. There is a filling defect from the anus to the rectosigmoid junction and the colon is distended.

in the groin or elsewhere. A roentgenogram taken after a barium sulfate enema showed a filling defect from the anus to the rectosigmoid junction and marked distention of the colon above (fig. 10). The Wassermann reaction was negative.

On January 27 I made an appendicostomy, and on February 15 I completely excised the rectum by the abdominoperineal method in one stage and made a permanent colostomy. The gross specimen is shown in figure 11 and the microscopic appearance is reproduced in figures 12 and 13. On March 19 Dr. Moses Paulson reported positive cutaneous reactions to two human strains of Frei antigen.

at the end of eight days. The patient was discharged from the hospital on April 19. The perineal wound was clean but not entirely healed.

Comment—My personal experience with venereal lymphogranuloma has been limited, and this is the first time that I have observed this disease in the rectum in the absence of involvement of the inguinal nodes. The absence of metastasis to the regional lymphatic nodes and to the liver notwithstanding the extensive filling defect in the roentgenogram and the large mass palpable from within the peritoneal cavity



Fig. 11—Photographs of the gross specimen in case 4. Note the narrow lumen, the ulceration of the mucosa and the thickened wall of the rectum. The fresh specimen had the consistency of leather.

could have suggested to me the possibility of a benign stricture of the rectum. In that event the diagnosis of venereal lymphogranuloma could have been confirmed before instead of after excision of the rectum and the operation confined to the establishment of a permanent colostomy.

Comment—Cases 5 and 6 were observed with Dr. Bloodgood prior to Oct. 21, 1935 and are the cases to which reference has been made.

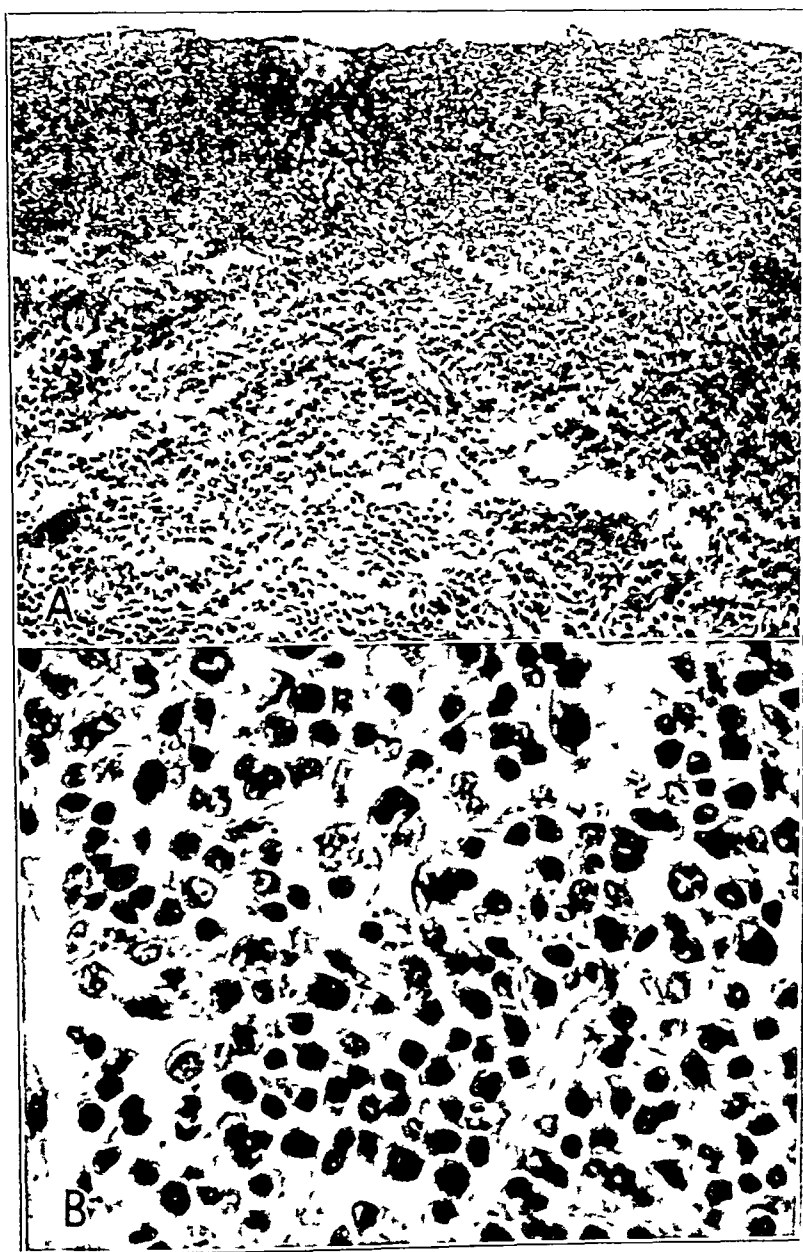


Fig 12 (case 4) — *A* low power photomicrograph of the ulcer in the rectum. Note the complete absence of glands, the rich cellular infiltration at the base of the ulcer, and the edematous stroma beneath showing plasma cell infiltration. *B* high power photomicrograph of the rectal wall beneath the base of the ulcer showing a rich infiltration of plasma cells in the edematous stroma.

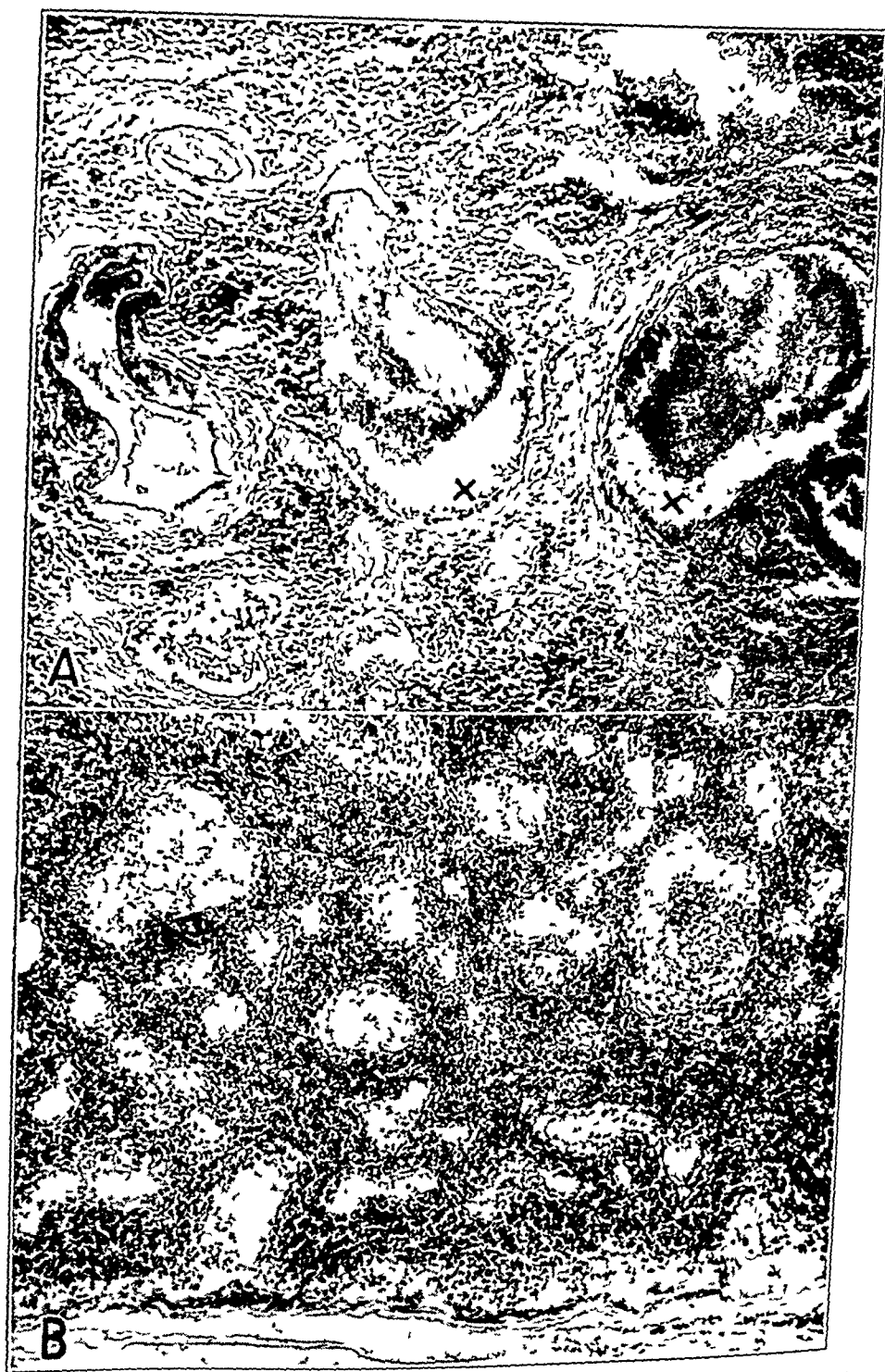


Fig 13 (case 4) — *A*, low power photomicrograph of the rectal wall beneath the area shown in fig 12 *B*. Sheets of plasma cells are present as in figure 12. Note particularly the marked dilatation of the lymphatic vessels (x-x). *B*, low power photomicrograph of a lymphatic node. Note the diffuse dilatation of lymphatic vessels.



Fig 14—Low power photomicrograph of a frozen section of the tumor in case 5. Note the irregular glands lined by hyperchromatic epithelial cells.



Fig 15—Low power photomicrograph of the tumor in case 6, diagnosed as adenocarcinoma. Above and to the left are remains of normal epithelium.

CASE 5—A W, a white woman aged 49, consulted the clinic Oct 23, 1933, bringing with her a section prepared from a bit of tissue removed from the rectum one week previously. The microscopic structure of this tumor is shown in figure 14. She had noticed blood in the stools for two and one-half years. Digital and proctoscopic examinations revealed an indurated ulcer 3 cm in diameter involving the posterior wall of the rectum, beginning at a point 3 cm above the sphincter. Dr Curtis F Burnum treated the tumor by the daily direct application of radium through a proctoscope. At the examination Feb 17, 1934 the ulcer was completely healed, and the patient was well on June 6, 1938.



Fig 16—Medium low power photomicrograph of the tumor in case 7, diagnosed as adenocarcinoma. Note the adenomatous structure of the tumor, the larger glands (above) lined by goblet cells with the nuclei at the bases and the smaller irregular glandlike structures (below) lined by epithelial cells with hyperchromatic nuclei.

CASE 6—J B F, a white man aged 53, consulted the clinic Feb 11, 1935 because he had had diarrhea and blood in the stools for three months. Examination revealed an ulcer 6 by 4 cm in the left lateral wall of the rectum, beginning at a point 3.5 to 4 cm above the sphincter. The microscopic structure of the tumor is shown in figure 15. Dr Curtis F Burnam treated the tumor by the direct application of radium and by external roentgen irradiation. The patient is well.

Comment—In view of these favorable results irradiation therapy was tried in the following 2 cases

CASE 7—F L O, a white man aged 52, consulted the clinic April 3 1937 because of constipation and blood in the stools. Both symptoms had been present for fourteen months. Hemorrhoidectomy had been performed six months previously. Examination revealed a mass just within the anal sphincter, which



Fig 17—Plain roentgenogram of the pelvis in case 7, showing the distribution of radon seeds

involved the sphincter and the anterior wall and both lateral walls of the rectum. The prostate was uninvolved. The microscopic appearance of the tumor is shown in figure 16. Dr. Curtis F. Burnam implanted radon seeds in the tumor and gave a course of external roentgen irradiation (fig 17). On February 10 Dr. Burnam applied radium directly to a small residual ulcer in which biopsy showed adenocarcinoma. Examination on May 25 revealed no evidence of recurrence.

CASE 8—F. B., a white woman aged 70, consulted the clinic May 11, 1938. Pain in the rectum and constipation had been present for nine months, occasional blood in the stools for two months. Examination revealed a lobulated mass 4 by 2 cm in the posterior wall of the rectum, beginning at a point 5 cm above the sphincter. The microscopic appearance of the tumor is shown in figure 18. My associate Dr. Eugene Covington treated this patient by direct application of radium and by external roentgen irradiation. At examination on June 13, 1938, approximately four weeks after the beginning of the irradiation therapy, no visible or palpable evidence of the nodular tumor remained. The appearance was that of a healing ulcer.



Fig 18—Low power photomicrograph of the tumor in case 8. At the left, normal glands; at the right, irregular glands with epithelial cells, showing hyperchromatic nuclei.

COMMENT

In spite of the fairly long duration of symptoms, the lesion in each of these cases presented the appearance of an operable carcinoma and for this reason it is with some hesitation that I present such recent experiences with irradiation therapy. Because the immediate results in these 4 instances have been so striking I have great hope that further experience will justify a trial of irradiation therapy before operation in all cases of early operable carcinoma involving the lower part of the

rectum My associates and I have not as yet had sufficient experience with irradiation therapy in cases of this kind to know exactly how the lesion should heal but in none of the few cases observed by us has a stricture occurred and the scars have been insignificant The numerous statements in the literature that adenocarcinoma is not a radiosensitive tumor are apparently incorrect because each of these 4 tumors proved to be an adenocarcinoma and yet completely disappeared under irradiation Whatever the ultimate results may be this fact cannot change

REVIEW OF UROLOGIC SURGERY

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(Concluded from page 169)

URETHRA

Staphylococcic Infections—Harkness and King³² said that when staphylococci are found in the genital tract, cultures almost always show them to be of the albus type. Although *Staph. aureus* is rarely found, when it is the infecting organism the suppuration is more extensive and profuse and there is greater constitutional disturbance than occurs with *Staphylococcus albus*.

Pathogenic organisms are distinguished from contaminating organisms by the fact that they are present in large numbers, are the sole or predominant organism and give a profuse cultural growth.

Staph. albus is the commonest cause of primary nongonococcal urethritis. Such infection is often venereal. The incubation period is usually longer than in cases of gonorrhea except when the infection is superimposed on urethritis chemically induced by the use of strong solutions for prophylaxis.

³² Harkness, A. H., and King, A. J. Staphylococcal Infections of the Genital Tract in the Male, *Brit. J. Urol.* **10**: 379-391 (Dec.) 1938.

There is a chronic type of staphylococcic urethritis in which the onset is insidious and the symptoms are mild it may be overlooked even when there are pronounced granular changes in the urethral mucosa. Staphylococcic urethritis is relatively a more common cause of stricture than is gonococcic urethritis. Secondary staphylococcic urethritis following gonorrhea is common. Repeated cultures should be made of the secretions from the prostate gland the seminal vesicles and Cowper's glands although the focal lesions responsible for persistence are often in the anterior portion of the urethra.

Thus, urethritis following trauma from injections of strong solutions careless or inefficient catheterization or urethral dilatation is usually abacterial at first but later shows *Staph. albus* on smear and on culture.

Urethral discharge caused by staphylococcic urethritis may be the only symptom of a serious lesion of the upper portion of the urinary tract, and this possibility should be borne in mind even if the patient states that there has been recent sexual intercourse. Obsessed with the possibility of venereal infection, the patient may overlook other symptoms of gradual onset and longer duration.

Treatment consists of through and through irrigations with any weak, warm and nonirritating antiseptic solution followed by urethral dilations. The new chemotherapy profoundly modifies the course of the disease, and sulfanilamide combined with the irrigations is effective. When sulfanilamide fails mandelic acid will frequently clear up the infection. Dilations followed by irrigations should be given once a week until urethroscopic examination shows them to be no longer necessary.

Prostatitis is the most common complication of primary staphylococcic urethritis, and urethral stricture may be a predisposing cause. The symptoms and clinical course of acute and chronic prostatitis prostatic abscess cowperitis seminal vesiculitis and epididymitis caused by the staphylococcus vary little from those caused by other pyogenic organisms.

Infection of these structures with the staphylococcus follows gonorrhea urethral instrumentation descending renal infections or operation (prostatectomy) or the infection may be blood borne. Harkness mentioned 2 cases of prostatitis in which the condition followed a crop of boils. In neither case was there a history of infection of the urinary tract or venereal exposure.

In the acute stage of infection of these structures sulfanilamide promptly relieves the symptoms. Acute prostatitis and cowperitis are likely to be more resistant to the drug as is chronic staphylococcic prostatitis although occasionally a dramatic cure may result.

Abraham³³ said that of the three types of staphylococci, *Staph aureus*, *Staph albus* and *Staph citreus*, the first is pathogenic, the second is mildly so and the third is not a pathogen. *Staph aureus* and *Staph albus* are almost always present in the skin and in the sebaceous glands. To change them from saprophytes to parasites there must be trauma, local pressure or irritating discharge on a moist surface. Such conditions often involve the female genitalia.

In 100 women suffering from urethritis and endocervicitis, smears and cultures showed staphylococci in the cervix and urethra in 52, *B coli* and diphtheroids in the cervix and urethra in 33 and staphylococci, diphtheroids and *B coli* in the urethra in 10 and in the cervix in 8 of these 10 patients. All of them, in addition, were examined for *Trichomonas vaginalis* but this was found in only 7 cases.

In children, infections of the genitalia exist as vulvovaginitis, because the glandular structures (Bartholin's gland, Skene's glands and the cervical glands) are not developed and because estrogen, which makes the vaginal epithelium resistant to infection, is absent.

In the vulvovaginitis of children, *Staph albus* and diphtheroids are present in 25 to 50 per cent of cases. The discharge is thick, yellow and not offensive like that in infections with *B coli* or *Trichomonas*. The lower third of the vagina is involved, and, although the external urinary meatus is inflamed, pain and increased frequency of urination are negligible. In adults these conditions are reversed.

Staphylococcic infections result in ductitis and Bartholinitis, urethritis, skeneitis and endocervicitis. Forty per cent of infections of Bartholin's glands are staphylococcic or streptococcic. Staphylococcic urethritis is commonly secondary to gonorrhea, as a primary infection it is surprisingly rare. Vaginitis is rare, but staphylococcic endocervicitis is common.

In the treatment of these conditions, chemotherapeutic and bacteriologic agents are valuable. Manganese butyrate given intramuscularly in doses of 1 cc of a 1 per cent solution every five days speeds up the disappearance of staphylococci from cervical and urethral smears. Abraham³³ said that in his hands the results of sulfamidamide therapy have not been impressive. Others have been more fortunate.

Formerly, because of the success of vaccine therapy, it was thought that the pathogenicity of staphylococci was due to endotoxins. Now it is known that they produce three toxins, alpha, beta and leukocidin, so that treatment by toxoids and antitoxin greatly augments ordinary vaccine therapy.

Antistaphylococcus serum is given intramuscularly in doses of 10 to 50 cc daily after a minute dose has been given to see if the patient is allergic.

³³ Abraham, J. J. Staphylococcic Infections in the Female Urethra and Genitalia, *Brit J Urol* **10** 392-399 (Dec) 1938.

Staphylococcus toxoid comes in two strengths the weaker being one tenth as strong as the stronger. A preliminary injection of 0.5 cc of the weaker toxoid is given subcutaneously, and if the reaction is not severe, 0.1 cc of the stronger is given a week later. The dose can be increased weekly.

For staphylococcal vulvovaginitis of children local treatment should consist in cleanliness, baths and mild germicidal irrigation. Over-treatment should be avoided.

For Bartholinitis the glands should be opened, drained, packed and allowed to granulate from the bottom.

Ductitis and skenitis are best managed by incising the ducts with a fine diathermy point.

For urethritis injections twice weekly of glycerin, 10 per cent strong proteïn silver and glycerin or 1 per cent mercurochrome are valuable. In cases of chronic involvement the urethra should be dilated and 1 per cent silver nitrate instilled.

Acute endocervicitis is best treated by swabbing the cervical canal with glycerin, and using glycerin tampons and vaginal douches of 2 per cent lactic acid. Local applications in chronic endocervicitis should be escharotic to be of any value. For the same reason, diathermy, if employed, must be used as a cautery.

If there are lacerations tracheloplasty is indicated.

Catheterization—Emmett³⁴ discussed the minimal armamentarium and the points in anatomy and technic which may be of value in cases of difficult urethral catheterization. The article is intended primarily for general practitioners. Emmett mentioned the fixed and relatively inelastic roof of the urethra and emphasized the importance of having the instrument hug the anterior urethral wall during catheterization. Sterile technic, adequate lubrication and good catheters are necessary. Slowness and gentleness, especially at the sphincters are essential. If the use of the soft rubber catheter is unsuccessful Emmett advocated successively the use of a coude soft rubber catheter with a hollow olive tip, the woven coude or bicoude catheter, a soft rubber catheter with a hollow tip over a wire stilet or a filiform guide followed by a woven catheter. The value of morphine and a sitz bath as relaxing agents is stressed. If all these methods fail anesthesia may relax the patient enough to allow passage of a catheter, thus being unsuccessful suprapubic drainage may be required. Proper use of the indwelling catheter is also considered.

³⁴ Emmett, I. L. Difficulties in Urethral Catheterization. *Am. J. Surg.* 40: 349-356 (May) 1938.

PROSTATE GLAND

Cancer—Kahler³⁴ studied 195 carcinomas of the prostate gland, 72 of which were diagnosed clinically and the diagnosis confirmed at postmortem examination and the remaining 123 of which were diagnosed after the death of the patient. The clinical diagnosis was based on palpation alone in 23 cases, was supported by biopsy in 30 additional cases and in 19 cases was determined by palpation plus demonstration of distant metastatic lesions. In only 4 cases was a small tumor described clinically, 3 of the tumors were proved microscopically to involve the entire prostate gland and only 1 to be a small carcinoma (1 cm in diameter). In this series the average age of the patients at the time of death was 68 years. The incidence of carcinoma of the prostate gland in men more than 50 years of age was 17.3 per cent. In only 3 cases in which the diagnosis was made clinically and 93 cases in which it was made at necropsy was the carcinoma confined to one lobe. In only 46 per cent of these was the posterior lobe the involved portion, as compared with 48 per cent in which the lateral lobes were involved and 6 per cent in which the anterior lobe was involved.

In only 53 per cent of the entire 195 cases was carcinoma recognized grossly at necropsy. Fifty-one per cent of the tumors were recognized because of increased consistency above the remainder or because of a yellowish white or hemorrhagic tint with or without increased consistency. The yellowish tint, which is due to fat and urochrome pigment, was present in only 21 per cent of the tumors. On microscopic study, Kahler³⁵ found that all the tumors were adenocarcinomas except 3 per cent, which were squamous cell malignant growths. The grading of the adenocarcinomas was as follows: grade 1, 19 per cent, grade 2, 50 per cent, grade 3, 27.5 per cent, and grade 4, 3.5 per cent. The incidence of the lower grades was greater in the localized tumors and in the lower age groups. The most important microscopic criterion of prostatic cancer is involvement of the perineural lymphatics. This was observed in 91 per cent of the cases and in 100 per cent of those in which the tumor was graded 3 or 4. The localized tumors, even the smallest ones, showed the same high incidence of perineural involvement, an important argument against the feasibility of local removal.

Kahler³⁵ found that in 51 per cent of the clinically or grossly recognized tumors metastasis had occurred by the time death took place. The points of metastasis, in order of their frequency, were the lymph nodes, lungs, pelvic peritoneum and bone. Direct extension occurred, in order of frequency, to the bladder, ureters, seminal vesicles and rectum. The incidence of metastasis increased markedly as the grade of the

³⁵ Kahler, J. E. Carcinoma of the Prostate Gland. Proc. Staff Meet., Mayo Clin. 13: 589-592 (Sept. 14) 1938.

lesion increased being 100 per cent in lesions of grade 4. The incidence of metastasis bore no relation to the size of the gland.

The association of atrophy and carcinoma was found to be incidental, as atrophy occurred in the same proportion of carcinomatous glands as of normal ones. Nodular hyperplasia also showed an incidental relation, as only 16.6 per cent of the localized tumors were found to have arisen from regions of nodular hyperplasia. Similarly, no relation existed between carcinoma and asymmetry, inflammation or calculi in the prostate gland.

Abscess—Tomassini³⁶ stated that the most common factors that cause abscess of the prostate gland are inflammation of the bladder and especially of the urethra. Prostatic abscess usually follows acute prostatitis, which may be diffuse or localized. Although all authors agree that gonorrheal urethritis is the essential factor, the micro-organism most frequently present is a staphylococcus.

Diagnosis is made mostly by rectal exploration, the results of which are interpreted in connection with the history as regards past infection, the subjective disturbances and the temperature. Most frequently the abscess opens spontaneously into the urethra or rectum. The treatment of choice when the collection of pus is considerable and when the general condition is such as to permit it is perineal prostatotomy.

An abscess is occasionally found before puberty when the gland has not acquired its special function. Two cases have been recorded in which the patients were young children, aged 4 years and 28 months respectively. The disposing factors are diabetes, gout, lymphatism, scrofula and arthritis. Chronic contusions, such as those caused by horseback riding, which provoke congestion of the veins of the small pelvis may awaken a latent infection, most often in the urethra. In addition the prostate gland feels the influence of all other causes of congestion such as sedentary habits, hemorrhoids, constipation and proctitis, all of which favor stagnation of blood in the venous plexuses of the small pelvis.

The organ is enlarged, hyperemic and edematous. The microscopic picture varies according to whether the parenchyma or the interstitial tissue is chiefly involved. In a large number of cases the origin is in the glandular lacunae. If the collection of pus succeeds in opening spontaneously through the urethra or rectum, spontaneous cure occurs. In other cases cure is slow and may be delayed by purulent or urinary fistulas. In rare cases the prostate gland may be overwhelmed by a grave and rapid suppurative process in which it and the surrounding tissues fall into a state of necrosis; in such cases the condition nearly always ends fatally.

³⁶ Tomassini, I. Sull' ascesso della prostata. Arch. ital. di urol. **15** 292-299 (June) 1938.

When the abscess fails to open spontaneously or when the opening is insufficient and the tumefaction has reached a considerable size, it must be opened surgically. It may then be approached by the hypogastric, rectal or perineal route. The last is preferable, with a bi-ischiatic incision made horizontally between the rectum and the urethra. The abscess is reached, opened, carefully drained and treated with suitable medication.

The first symptoms are urinary and consist of frequency and urgency of voiding, soon followed by a sense of weight and tension in the prostate gland and rectum. The temperature is high, and chills sometimes occur. Rectal examination is extremely painful, a finding that distinguishes an abscess from a tumorous condition or hypertrophy. Fluctuation is a late finding. Frequently the sulcus cannot be found, and the gland feels like a single mass. The urine is only slightly cloudy until perforation into the urethra occurs, which causes the urine to become purulent. Such an opening may be spontaneous or may occur during catheterization or rectal exploration.

Emmett, Lovelace and Mann³⁷ carried out a series of intraprostatic injections of sclerosing solutions. The late result of injection of such solutions into the prostate glands of dogs was a definite reduction in the size of the lobe into which the solution had been injected. The reduction seemed to be associated with increase in the connective tissue stroma, possibly with some reduction in size and number of the prostatic acini. There was no untoward reaction, and symptoms referable to the urinary tract were not observed in any of the experiments. The article is a report of animal experimentation only, and its clinical application in any type of case is not suggested until further experimentation has been done. The work, however, does furnish a new field for thought, and the method will bear further investigation.

Hypertrophy—According to Retlev-Abrahamsen and Aalkjaer,³⁸ many patients who have prostatic hypertrophy and who do not respond to treatment by drainage and forced fluids are considered genuinely uremic when, in fact, they are suffering from pseudouremia or nephrogenous acidosis.

This condition can be recognized by a determination of the value for plasma bicarbonate, which is normally 25 to 30 mg per liter of blood. When this falls below 19 mg per liter there are nausea, loss of appetite and dryness of the tongue, the patient cannot drink and is lethargic. When the value for bicarbonate is less than 14 mg per liter, typical

37 Emmett, J. L., Lovelace, W. R., II, and Mann, F. C. Intraprostatic Injection of Sclerosing Solutions. An Experimental Study, *J. Urol.* **40** 624-628 (Nov.) 1938.

38 Retlev-Abrahamsen, H., and Aalkjaer, V. The "Pseudouremia" of Patients with Prostatic Hypertrophy—The Nephrogenous Acidosis, *Brit. J. Urol.* **10** 231-236 (Sept.) 1938.

acidotic coma appears, with Kussmaul respiration. The clinical evidences of nephrogenous acidosis in cases of chronic prostatism are anhydremia, hypochloremia, fever, dyspepsia and senility.

Examination for and treatment of nephrogenous acidosis is indispensable to surgical treatment of the prostate. Treatment consists in the administration intravenously of 1.3 per cent (isotonic) sodium bicarbonate solution. The amount given is based on the blood value for bicarbonate and the body weight and is determined by use of the nomogram of Palmer and van Slyke. If according to this nomogram the patient is to be given 3 liters of a 1.3 per cent solution of sodium bicarbonate, 1 liter of the solution is given each day for three days and an analysis of the blood is made on the fourth day. In this way alkalosis and tetany are avoided.

Of 123 patients with prostatic hypertrophy treated by Retley-Abrahamsen and Aalkjaer³⁸ since January 1936, one third were found to have nephrogenous acidosis. Appropriate treatment reduced the values for blood urea, corrected the anhydremia and permitted operation in a few days on patients who formerly had been considered hopelessly uremic.

Endocrine Therapy—Walther and Willoughby³⁹ stated that prostatic hyperplasia can no longer be regarded as an independent entity, it is inseparably bound up with endocrine changes affecting the pituitary body and the testis.

In cases of early prostatism or in cases in which for some serious physical disability caused by any type of prostatic obstruction operation seems inadvisable, androgens should be given conscientious trial. The disadvantage of this mode of treatment is that, as with insulin therapy, one must continue a maintenance dose, therefore, contact with the patient for an indefinite period is necessary, and massage is usually indicated. Preparations of androsterone and testosterone propionate for oral and intramuscular use are available for such therapy.

Fifteen patients with benign prostatic hyperplasia have been treated with these substances by Walther and Willoughby³⁹ during the past two years with clinical improvement of their symptoms.

Moore and McLellan⁴⁰ made a histologic study of the effect of androgen and estrogen on the prostate gland of the human being. They stated that the injection of 285 to 1,125 mg. of testosterone propionate in twelve to ninety-five days results in no significant restoration of the involuted prostate gland of senility and causes no observable

39 Walther H. W. E. and Willoughby R. M. Hormonal Treatment of Benign Prostatic Hyperplasia. *Tr. Southeast. Pr. Am. Urol. A.* Nov. 5, 1937, pp. 63-72.

40 Moore R. A. and McLellan A. M. A Histological Study of the Effect of the Sex Hormone on the Human Prostate. *J. Urol.* 40: 641-657 (Nov.) 1938.

alteration in the histologic appearance of the tissues formed in benign hypertrophy. The injection of 15,000 to 140,000 international units of estradiol benzoate in ten to thirty-one days produces conspicuous alteration in the urethral and ductal epithelium but little if any change in the tissues of benign hypertrophy.

Infarction—Hubly and Thompson⁴¹ found a single study (Abeshouse 1933) of prostatic infarction in a review of the literature. The authors' report is based on a clinicopathologic study of 10 cases of prostatic infarction. Hubly and Thompson stated the opinion that function of the prostatic portion of the urethra is influenced by volumetric changes in the prostate gland and that changes of this type resulting from infarction may produce symptoms. The symptoms produced depend on the stage of infarction. During the early stage, when swelling is most pronounced, varying degrees of urinary obstruction, including acute urinary retention, may develop. In the later stage, cicatrization and contraction occur and the patient voids satisfactorily. This sequence of events, perhaps repeated on several occasions, may explain episodes of retention followed by more or less spontaneous relief of symptoms. The final stage of prostatic infarction may be manifested by regions of fibrosis, which are commonly found in the prostate gland. The 10 cases reported are considered in some detail. Prostatic tissue was obtained at necropsy in 6 of these cases and by transurethral resection in the remaining 4.

Trauma (such as that caused by prostatic massage), difficult urethral catheterization, prostatic resection and electrocoagulation may be factors in the production of infarction. Abeshouse has suggested that adenomatous hyperplasia, by distortion of the intraglandular blood supply, may cause infarction. Infection, circulatory stasis and arteriosclerosis may also be etiologic factors.

TESTICLE

Ectopy—Jones and Lieberthal⁴² stated that only 103 cases of perineal testicle have been reported. The exact mechanism of normal descent of the testis is not known, although the subject has been widely discussed and many elaborate hypotheses have been offered. It is known that before migration of the testes occurs, in early fetal life these glands occupy primarily a site in the lumbar region on either side of the vertebral column, in front of the psoas muscle and internal to the kidneys. At the beginning of the third month they begin to descend along the posterior abdominal wall, carrying with them their vascular pedicle and

41 Hubly, J. W., and Thompson, G. J. Infarction of the Prostate. Its Clinical Significance, Proc. Staff Meet., Mayo Clin. **13** 401-403 (June 29) 1938.

42 Jones, A. E., and Lieberthal, F. Perineal Testicle, J. Urol. **40** 658-665 (Nov.) 1938.

pushing ahead of them the parietal peritoneum which is to constitute the processus vaginalis. As they gradually move downward they occupy successively positions in the abdominal, iliac and inguinal regions, until they finally reach their permanent bed within the scrotum just before or occasionally, soon after birth.

A testis may become arrested at any of the first three stages, it is then known as an undescended testis. In addition to such arrests, however, there are found, in much rarer instances deviations in migration which prevent the testicle from pursuing its normal course, deflecting it from its appointed path and landing it in some spot from which it cannot possibly reach the scrotum. When this occurs, the testis is known as ectopic. Unlike the testis that remains undescended, which is frequently the victim of some abnormality, the ectopic testis according to most authorities is usually normal and perfect in its development.

Ectopic testicles are of four varieties: (1) superficial, inguinal or interstitial, (2) penile, (3) perineal and (4) crural or femoral. The perineal testis lies in practically the same position in all cases. It is always found between an imaginary line in front passing behind the root of the scrotum and a similar line passing in front of the anus laterally; it is always outside the line of the raphe; it has never been known to lie behind the bi-ischiatic line, which passes anterior to the anal orifice. No adhesion of the testis to the tissues covering it has ever been observed. Frequently it can be slipped about with the greatest ease sliding under the finger and often displaying sufficient mobility to pass under pressure into neighboring regions.

Treatment is surgical. The gland has gone into the wrong fascial pocket, and only surgical measures can restore it to its rightful bed. The cord in such a case is always long enough for this transplantation and the operation is easily executed. If possible it should be carried out before the boy subjects the organ to trauma which may easily occur with the testis in this perineal position. The operation should not, however, be carried out on children under the age of 3 years unless the condition is causing symptoms.

Jones and Lieberthal reported the case of a 17 year old boy. There was a mass about the size of a plum situated to the right of and close to the anal sphincter. While this mass was somewhat tender on palpation there was no history of pain or discomfort, although the boy had taken part in various athletic games at school. The right side of the scrotal sac was empty and somewhat shrunk. At operation a normal testis was separated from its gubernaculum and placed in the scrotum.

Tumor—McDonald⁴³ reported that approximately 142 cases of chorionepithelioma of the testes have been reviewed. He reported an

⁴³ McDonald S. Jr. Observations on Chorionepithelioma Testis with Record of a Case. *Am. J. Cancer* 34:1-14 (Sept.) 1938.

additional case. The patient was a man 24 years of age. The right testis was three times the normal size. A diagnosis of teratoma having been made, the testis was removed. Histologic examination proved that the growth was a teratoma with chorionepitheliomatous elements. The qualitative Zondek-Aschheim reaction was positive eleven days after orchidectomy. Two months after operation the Zondek-Aschheim test showed 30,000 mouse units of gonadotropic substance per liter. The breasts had become moderately enlarged. The condition of the patient rapidly became worse, and he died three months after the operation. Necropsy showed multiple metastatic lesions, especially in the lungs and kidneys.

McDonald considered the histogenesis of the tumor and concluded that, although the tumor arises through malignant differentiation of a teratoma, endocrinologic observations support the belief that testicular chorionepithelioma is morphologically identical with uterine chorionepithelioma. He suggested that a quantitative Zondek-Aschheim test is essential in the investigation of testicular tumors and that correlation of the amount of gonadotropic substance present in the urine and the histologic characteristics of the growth may afford valuable information as to the nature and source of gonadotropic hormones.

Ormond⁴⁴ reviewed the symptoms and results in cases of torsion of the testicle and reported 12 new cases. He emphasized the importance of prompt recognition of this condition and stressed the following elements in the diagnosis: (1) the age of the patient [in this series 8 patients were less than 23 years of age, the youngest being 4 years old and 5 others being adolescents], (2) the sudden onset, (3) the severity of the pain, (4) the absence of history or evidence of genitourinary infection, (5) the position of the affected testicle in the scrotum, (6) the position of the epididymis with reference to the testicle, (7) the tenderness of the testicle, and (8) Prehn's sign.

Finally, Ormond emphasized his conclusions regarding treatment. He stated that in an acute attack prompt operation offers the best chance of a healthy testicle, that although an attack is relieved by manual or spontaneous detorsion, operation should be done soon to prevent recurrence, and that if because of torsion a testis has become atrophic or has been removed, operation should be done on the remaining testis to prevent a like fate befalling it.

Hypertrophy—Zide⁴⁵ studied 19 cases of unilateral testicular abnormality occurring after puberty. He wished to determine whether compensatory hypertrophy of the remaining testis actually occurred. In

44 Ormond, J. K. Torsion of the Testicle, *J. A. M. A.* **111** 1910-1914 (Nov. 19) 1938.

45 Zide, H. A. Does Compensatory Hypertrophy of the Adult Human Testis Occur? *Proc. Staff Meet., Mayo Clin.* **13** 268-269 (April 27) 1938.

17 of these cases unilateral testicular atrophy occurred after the orchitis of mumps orchidectomy for unknown reasons had been performed on the remaining 2 patients. Measurements of the length and width of the unaffected testis of each patient were made with a caliper. As a control the testes of 29 normal adult persons were measured. The testes of the control series averaged 3.8 cm. in length and 2.3 cm. in width. The uninvolved testes in the 19 cases of unilaterally atrophic or absent testes averaged 3.9 cm. in length and 2.5 cm. in width. The difference in size between the normal and the abnormal groups was found to be of no significance in this small series. The measurements of the largest testis in each group were within the normal limits for length but in both groups slightly exceeded normal width. It is concluded that the testis of the adult human being does not undergo any appreciable compensatory hypertrophy after atrophy or removal of its mate.

Cabot stated that many teachers have said that compensatory hypertrophy does occur after the loss of one testis in adult life, because it is known that this phenomenon occurs in the case of the kidney. He stated, however, that the cases are different, as it is important in the economy of the body that more renal tissue should be available for use under stress. Although this work is practically convincing to Cabot that the alleged occurrence of hypertrophy of the testis in the adult lacks a sound basis in observed fact, it does not answer the question of increased growth of a testis when its fellow is lost during childhood.

URINARY CALCULI

Pyrh and Fowweather⁴⁶ discussed the etiologic problems presented by calculi in recumbent patients.

The calculi at first are pasty masses deposited in the calices or in the pelvis, these "mud-stones," as they have been termed may remain in this condition or may solidify into true calculi. The authors stated the opinion that the kidney itself suffers no permanent damage. The calculi vary to some extent in composition, which is largely dependent on the reaction of the urine, but all writers agree that phosphates of calcium are the principal substances found in these calculi.

Calculi in recumbent patients have been attributed to suppuration of bone. Urinary infection has been regarded by some authors as essential but, although frequently found such infection is by no means always present. The essential condition in the production of calculi on recumbency is the establishment in the urine within the kidney of a sufficient concentration of calcium ions together with the necessary reaction to allow the calcium to be precipitated as a salt in either the

⁴⁶ Pyrah, L. N., and Fowweather, F. S. Urinary Calculi Developing in Recumbent Patients, *Brit. J. Surg.* 26: 98-112 (June) 1938.

larger tubules or the calices of the kidney. The processes which create this condition are varied, and no doubt several come into play in any given case. Pyrah and Fowweather stated:

The principal etiologic factors are (1) release of calcium salts from the bones into the bloodstream as a consequence of (a) generalized decalcification of the entire skeleton as a result of immobilization, (b) localized decalcification of bone near the site of the injury or infection. The calcium salts so released are excreted mainly by the urine, (2) increased concentration of calcium salts in the urine because of dehydration resulting from isolation and low intake of fluid, thus favouring precipitation, (3) stasis and inadequate renal drainage because of the enforced recumbent posture, (4) dietetic factors (a) influence of diet and drugs on the reaction of the urine, (b) total amount of calcium taken by mouth, (c) deficiency in vitamin A and (d) possibly hypervitaminosis D, (5) infection (a) in the urinary tract, (b) ascending urinary infection in the female, (c) in other parts of the body, that is, in bone and (d) constipation.

In most of the recorded cases, renal calculi have been found to have developed after many months or years of recumbency. There are theoretic reasons for supposing that their development actually commences early in recumbency, and it is probably true that if a stone does not develop early it will not develop at all. The first symptom is usually hematuria, and it occurs soon after the patient has been turned from the dorsal position to the ventral, the hematuria is often profuse. Renal colic occurs in a considerable number of cases with or without bleeding.

The aim for the future must be prevention of the formation of calculus and of urinary infection. Decalcification of bone, dependent as it is on relative hyperemia, cannot be absolutely prevented, but it can be minimized by routine daily massage and active movements of the limbs not actually splinted. Large amounts of fluid must be supplied to the patient at regular intervals throughout the day. The fluid should either be neutral in reaction (such as water) or should be such that "ash" from the solid residue will be acid in reaction. In order that stasis of urine containing solid particles may not occur in the renal pelvis the recumbent patient should be turned (either by tilting him to one side or by turning him into the prone position) at fairly frequent and regular intervals. In order to render the urine acid and thus maintain solution of the urinary calcium phosphate, a diet yielding an acid "ash" should be adopted as a routine. Vitamin A should be prescribed, although deficiency of vitamin A as an etiologic factor is not yet finally established. Constipation should be avoided by the use of aperients if necessary. Absolute cleanliness, particularly of the vulval and anal region of females in plaster casts is vital if ascending infection is to be prevented. Prophylactic examination of the urine for erythrocytes should be made once each month and their presence should be taken to indicate the necessity for active therapeutic measures against a possible calculus.

The object of treatment is to cause the renal calculi to go into solution or to disintegrate into tiny particles which will pass down the ureter and be excreted. If the urine is not infected, operation is contraindicated as the stone can usually be made to disappear.

Calculi associated with gross infection of the urine require surgical intervention for their removal. Calculous pyonephrosis and calculous anuria form absolute indications for operation.

Chemical Composition of Urinary Calculi—Jensen and Thygesen⁴⁷ examined 35 phosphatic urinary stones to determine their chemical structure. They carried out systematic qualitative analysis of all the stones. In a number of cases a quantitative analysis was also done and an acid-basic ash determination made. The following substances were found in the stones: (1) $\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$, (2) a colloidal phosphate of calcium with imperfect, apatite structure, containing 3 to $3\frac{1}{2}$ equivalents of calcium per mol of phosphoric acid and some water, and (3) $\text{Ca}_3(\text{PO}_4)_2$.

The substances numbered (1) and (2) are the ordinary ingredients of phosphate stones and are more often found mixed than in a pure state. Two stones consisted entirely of $\text{Ca}_3(\text{PO}_4)_2$. Calcium carbonate, normal magnesium phosphate and the secondary calcium phosphates, which are often supposed to form phosphate stones, could not be found.

UROLOGIC DIAGNOSIS

Scholl⁴⁸ stated that various urologic conditions greatly resemble the clinical picture and not uncommonly lead to the diagnosis, of chronic glomerulonephritis. The most common conditions are infection, obstruction and certain metabolic disturbances. The majority of these diseases are readily recognized if a complete urologic examination is carried out. The similarity of the various urologic conditions to chronic glomerulonephritis leads to a diagnosis of nephritis. The fear that urologic instrumentation may be followed by serious reactions frequently prevents a complete study that would indicate the true nature of the lesion. Such a fear is in most cases not warranted as reactions rarely follow cystoscopic procedures with the rapid accurate methods now employed and the use of recently devised innocuous urographic materials. Carefully and gently carried out such examinations cause no trouble even to a patient with severely damaged kidneys.

In all cases in which there is the slightest doubt as to the diagnosis the patient should be given the benefit of a complete urologic investigation. If this is thoroughly carried out a small but definite group of

47. Jensen, A. T. and Thygesen, I. E. Ueber die Phosphatkonkremente der Harnwege, *Ztschr. f. Urol.* **32** 659-666 (Oct.) 1938.

48. Scholl, A. I. Urologic Conditions Simulating Chronic Glomerulonephritis. *I. A. M. A.* **111** 1421-1427 (Oct. 15) 1938.

patients in whose cases a diagnosis of chronic glomerulonephritis has been made will be found to have conditions that can be partially or completely relieved

ANESTHESIA

Ferrin⁴⁹ studied a series of controlled clinical cases in which diothane hydrochloride had been used for urethral anesthesia both prior to and subsequent to urethral trauma. In 100 cases only 2 reactions were noted, and both of these were mild, subsiding without treatment. Neither diothane hydrochloride nor any other anesthetic agent should be used in the traumatized or normal urethra without careful supervision. In cases in which the use of an anesthetic agent locally is deemed desirable in spite of trauma, diothane hydrochloride appears to be the anesthetic of choice. The prolonged relief from pain following the use of diothane hydrochloride in the urethra is extremely valuable.

Alken⁵⁰ made a resumé of the experience of the large urologic clinic in Berlin (formerly headed by Prof. A. von Lichtenberg, now by Dr. Heckenbach) with peridural anesthesia in the last three years. In that time, nearly 2,500 urologic operations have been done with the use of peridural anesthesia. This anesthesia, which is connected with the names of Dogliotti, Gutierrez and Kraas, is based on the following principle:

The anesthetic reaches the sensory nerves in the spinal canal outside the dura mater, causing anesthesia which has the completeness and advantages of spinal anesthesia without its drawbacks. The technic is simple. As an anesthetic agent, Alken⁵⁰ recommended a 2 per cent solution of pontocaine hydrochloride to which is added 15 drops of 1:1,000 epinephrine hydrochloride to each hundred cubic centimeters. The patient sits on a table with the head bent toward the knees as for spinal anesthesia. The needle is inserted in the midline. The mandrin is removed when the needle has gone 1 cm. deep, and a 10 cc. syringe filled with physiologic solution of sodium chloride is then fitted on the needle. The needle is made to advance slowly toward the spine while the operator is attempting to inject the saline solution. Nothing can be injected as long as the point of the needle is passing through the ligamentum flavum. As soon as the point of the needle comes into the peridural space, the pressure of the saline solution in the syringe falls to zero and the solution flows in freely, indicating that the point of the needle is in the peridural space and is pushing the dura mater ahead of it, reducing the chance of its perforation. Five cubic centimeters of the anesthetic solution is now slowly injected. This would be about the

49 Ferrin, J. W. Use of Diothane Hydrochloride in Urologic Cases, *J. Urol.* 40: 666-671 (Nov.) 1938.
50 Alken, C. E. Peridural Anesthesia, *Ztschr. f. Urol.* 32: 649-659 (Oct.) 1938.

correct amount for spinal anesthesia. Ten minutes later another 10 cc is injected if the first injection was correct and has not produced spinal anesthesia. After another ten minutes the remainder 10 cc is injected. The total dose, therefore, is 25 cc. To a small patient it is better to give only 20 cc, to a large person 35 to 40 cc. Thirty minutes after the first injection the anesthesia is complete. The anesthesia is best near the segments where the injection has been made. There is usually complete relaxation of the whole musculature. The site of injection for operations on the kidney and the upper portion of the ureter is in the interspace between the twelfth dorsal and the first lumbar vertebra, for the rest of the ureter, between the first and the second lumbar vertebra and for the bladder, prostate gland and genitalia, between the second and the fourth lumbar vertebra. The anesthesia lasts for two and one-half to three hours. During the whole period of anesthesia the general condition of the patient remains satisfactory. In the first minutes there is usually a slight rise in blood pressure but after twenty minutes the pressure falls 10 to 15 mm of mercury below the original level. Alken⁵⁰ often adds a mild narcosis induced by an intravenous injection of 1 cc eukodal-scopolamineephedrine (Merck).^{50a} This anesthetic is used at the Berlin clinic in every procedure for which good anesthesia is needed, from painful cystoscopic procedures to the most difficult resections and plastic operations. Age, diseases of the heart and diseases of the circulatory system are not contraindications.

There is only one grave danger in peridural anesthesia that is, perforation of the dura mater, which may pass unnoticed. If the perforation is clear and spinal fluid drops out of the needle spinal or general anesthesia must be used. Inducing anesthesia by injection into a segment above or below should not be attempted as the perforation in the dura does not close at once. In some old patients the dura mater is not elastic, so that the point of the needle may cause some trauma or may partially penetrate the dura. In this case the anesthetic agent may slowly penetrate into the spinal canal, causing late shock. As the amount of pontocaine which enters the canal is small, the shock quickly wears off after administration of a stimulant and the operation can be performed. This penetration of the dura has happened 11 times in the last 1 000 cases.

In Alken's⁵⁰ opinion, peridural anesthesia is the ideal method for the urologic surgeon, because it combines simple technique, harmlessness, good effect and long duration and is suited for all urologic procedures from cystoscopic examination to major operations.

^{50a} Eukodal is dihydrooxycodone hydrochloride. ephedrine is an isomer of ephedrine.

URINARY EXTRAVASATION

Ravenel⁵¹ discussed extravasation from the lower portion of the urinary tract. First he briefly reviewed the anatomic facts which directly influence its course. These are the fascial planes. The superficial perineal fascia consists of two layers, superficial and deep. The deep fascial layer forms a thin aponeurosis of considerable strength, continuous with the dartos of the scrotum, with the fascia of the penis and with Scarpa's fascia on the anterior surface of the abdomen, on either side it is firmly attached to the outer lip of the ischiopubic ramus. Posteriorly this deep layer curves around the superficial transverse perineal muscles to blend with the base of the triangular ligament.

The triangular ligament, or urogenital diaphragm, is composed of two layers. The structure stretches almost horizontally across the pubic arch, so as to close in the front part of the outlet of the pelvis. The superficial layer is separated from the subpubic ligament by an oval opening for the transmission of the dorsal veins of the penis.

The posterior layer of the triangular ligament is really a continuation of the pelvic fascia across the pubic arch.

The fascia of Denonvilliers is an aponeurotic structure which is attached to the tip of the prostate gland and the triangular ligament and passes upward between the rectum and the prostate gland, bladder and seminal vesicles. It sends an investment to the seminal vesicles.

Buck's fascia forms a dense fibrous investment of the corpora cavernosa and corpus spongiosum in a figure-of-eight sheath which terminates anteriorly at the base of the glans penis and is delimited posteriorly by the triangular ligament, where it is in apposition with Colles' fascia. It is continuous above with the suspensory ligament of the penis. In Buck's original article he described the fascia as continuous with Colles' fascia, but Wesson, by means of injection experiments to simulate extravasation, found evidence that Colles' fascia, although rather adherent to Buck's fascia at the base of the penis, passes down separately from Buck's fascia and envelops the entire penis except the glans.

The clinical evidence of extravasation of urine from the lower portion of the tract varies with the site of rupture through which the urine escapes.

The site of rupture in the urethra is indicated by the course taken by the extravasating urine. Extravasation occurring from the pendulous portion of the urethra, when not rapid, may ulcerate through the fascial planes and form a fistula, or it may pass forward along the corpus spongiosum and involve the glans penis.

⁵¹ Ravenel, I. J. Extravasation from the Lower Urinary Tract, *Tr. South-west Br., Am. Urol. A.*, November 1937, pp. 57-62.

When rupture of the urethra takes place in that part included between the attachments of the scrotum and the anterior layer of the triangular ligament, usually the bulbous portion, the course of infiltration is directed by the deeper layer of Colles' fascia. This is the common site of rupture of the urethra when infection and obstruction are the etiologic factors. The extravasating urine here being limited by the deeper layer of Colles' fascia it fills first the perineum just posterior to the scrotum, then it proceeds up over the symphysis to the abdominal wall infiltrating beneath Scarpa's fascia.

Because of the close fusion between Colles' fascia and Buck's fascia at the base of the penis laterally and interiorly it is usual that the extravasation does not at first involve the penis. After reaching the abdominal wall however it descends to and involves the penis.

Rupture of the membranous urethra with extravasation between the layers of the triangular ligament is unusual and is rather difficult to diagnose in the early stages. Generally it is not until one layer of the triangular ligament gives way or until the extravasating urine reaches and emerges through the subpubic hiatus in the anterior layer that definite symptoms appear. When this occurs the course is the same as when the bulbous urethra ruptures. Should the posterior layer give way, the urine may either follow the course of the rectum and appear at the anal perineum or pass up and invade the prevesical space.

Rupture of the urethra posterior to the deep layer of the triangular ligament is generally the result of trauma such as is often seen in cases of fracture of the pelvis.

The prognosis depends as much on an early diagnosis as on proper surgical treatment.

Ravenel observed a series of 57 cases with a recovery rate of 65 per cent. The penis alone was involved in 7 cases, the perineum alone in 1, the perineum and scrotum in 5, the scrotum alone in 3 and the scrotum and penis in 16. Extensive infiltration of the perineum, scrotum, abdominal wall and penis was present in 23. There were 2 cases of traumatic rupture of the membranous urethra with extravasation between the layers of the triangular ligament.

Early operation is imperative to divert the stream of urine from the rupture and to provide free incision and drainage of the infiltrated portions. In 47 of the cases external urethrotomy was performed, in 3 suprapubic cystostomy and in 6 drainage by catheter. In 1 case operation was not done, the patient having died within an hour after admission to the hospital.

Ravenel based his preference for the perineal approach on the following facts: (1) there is dependent drainage; (2) there is less shock.

and (3) there is avoidance of contaminating the prevesical space with the gas-producing anaerobic organisms so often found

DRUG AND FEVER THERAPY

Elkins and Krusen⁵² mentioned the decline in the use of fever therapy for gonorrhea since the advent of sulfanilamide. A small group of patients who do not show a satisfactory response to sulfanilamide, however, are still treated by artificial fever. The authors cited 2 cases of gonorrheal infection in which artificial fever therapy failed to effect a cure but treatment with sulfanilamide was successful. They also reported 10 cases in which fever therapy was employed, in all of which an adequate amount of sulfanilamide had been given previously without producing the desired result. All but 1 of the patients were cured after the fever treatments.

Elkins and Krusen stated that recently sulfanilamide combined with artificial fever therapy has been employed. They considered Ballenger's plan of combined treatment, giving 80 grains (5.17 Gm.) of sulfanilamide for two days before artificial fever therapy was instituted. The temperature of the body was raised to 103 or 104 F. for a period of three to four hours. Ballenger reported good results from the use of this combination of methods, although Kendell stated the opinion that the combined treatment has little more effect than fever therapy alone.

Elkins and Krusen reported only 2 clinical remissions following the use of a combination of sulfanilamide therapy and five hour sessions of artificial fever at 106.7 F. in a series of 10 cases. They did not feel that from this series they could draw definite conclusions, however, they concluded that fever therapy, with or without sulfanilamide therapy, will continue to be an important adjunct in the treatment of certain resistant types of gonorrhea.

Cook⁵³ stated that, although the gonorrheal patients seen at the Mayo Clinic are likely to have the more "difficult" types of infection, cure of more than 90 per cent of these patients was obtained by the use of sulfanilamide alone or in combination with local treatment. If, after trial of the drug for ten days, there has not been definite improvement, fever therapy must be considered and will prove of great benefit. Time alone will tell whether treatment with sulfanilamide and artificial fever has any advantage over fever therapy alone.

⁵² Elkins, E. C., and Krusen, F. H. Fever Therapy in Resistant Gonorrhea with Especial Reference to Its Relationship to Sulfanilamide Therapy of Gonorrhea, *Proc. Staff Meet., Mayo Clin.* **13** 299-303 (May 11) 1938.

⁵³ Cook, E. N., in discussion on Elkins and Krusen.⁵²

Emmett⁵⁴ called attention to the fact that the intravenous administration of mercurochrome has given disappointing results in the treatment of infections of the blood stream, however, small doses of this drug have been found useful in the management of acute pyelonephritis. Emmett mentioned the work of Braasch and Bumpus in 1926, in which reactions occurred in a large percentage of cases in which even a relatively small dose of mercurochrome was given intravenously. In most cases of acute pyelonephritis observed by Braasch and Bumpus the temperature returned to normal after the drug was given. In 28 of 69 cases in which the temperature was elevated on administration, the temperature returned to and remained at normal. There was no effect other than this antipyretic action. Two deaths were reported.

The constant need for some therapeutic agent to terminate a severe septic temperature in cases of protracted acute pyelonephritis gradually led to a reconsideration of the drug. Because the amount of mercury present in the blood stream during the administration of mercurochrome was shown to be exceedingly small, the effect has been felt to be non-specific. If this were true, a smaller dose was thought to be of probable value. Accordingly a small dose of 5 to 10 cc. of a 1 per cent solution has been used to terminate the high temperature associated with acute pyelonephritis.

Emmett stated that since 1933 mercurochrome has been used thus in about 125 instances with only 1 known (moderate) reaction. The administration is made usually by diluting it with 500 cc. of physiologic solution of sodium chloride. The response is usually prompt and dramatic.

Emmett analyzed the results in 34 cases in which forty intravenous injections of mercurochrome were given. Valuable conclusions were drawn in spite of the evident inaccuracies. In some cases of high post-operative temperature when the cause of the fever was in doubt mercurochrome was administered. In crises of the fever occurred it was felt that the diagnosis of acute renal infection could be made. The treatment was given in 22 cases of acute pyelonephritis in 10 of which the condition was a postoperative occurrence. In 20 of these cases the fever was decreased in 18 by crises. In 8 of these the fever recurred. In 5 of these 8 a second injection of mercurochrome was given and resulted in diminution of fever in 4 instances.

Emmett concluded that acute pyelonephritis is one condition in which the intravenous administration of mercurochrome may be expected to be effective. Although its only action is antipyretic it may prove to be a life saving measure in the occasional case in which a septic fever threatens the life of a patient. In a large percentage of cases the acute

⁵⁴ Emmett I. L. The Antipyretic Action of Intravenous Administration of Mercurochrome in Acute Pyelonephritis. *J. Urol.* **40** 312-318 (Aug.) 1938.

phase of the disease is terminated, however, the urinary infection must be eradicated subsequently by other chemotherapeutic means

Strauss⁵⁵ called attention to the beneficial effects of the combination of calcium and bromides on inflammation of the uropoietic systems of nervous patients. He used the preparation calcibronat "Sandoz"

VAGINITIS

Schauffler, Kanzler, and Schauffler,⁵⁶ in a review of their cases of vaginitis in infants, stated that their experience with distention with silver nitrate ointment in 99 cases, vaginal application of amniotin (an estrogen) in 31 cases, insertion of pyridium suppositories in 19 cases and various other methods in smaller series leads to the conclusion that the use of amniotin by vaginal application is the most satisfactory method of management they have used

Their study includes 261 cases in which sulfanilamide was administered orally. The results and opinions indicated that the method is unsatisfactory as used at present. The reason may be that administration of the drug is inadequate or inconstant. The desired low pH of the vaginal secretions may be important in relation to the ineffectiveness of sulfanilamide. Meticulous care during treatment requires hospitalization, a disadvantage. The method as used thus far apparently does not compare favorably with other available methods.

Evidence from a rather painstaking study indicates that the endocervix is seldom an important factor in relation to vaginitis and is practically never such a factor when the patient is a young child.

HEMOSTASIS

Rannert⁵⁷ studied the hemostatic effect of vitamin P in different urologic conditions. She found that after intravenous injection of 55 mg, or after oral administration of 100 mg, of vitamin P, bleeding from any source in the urologic tract could be diminished or stopped. Other examinations revealed that the hemostatic effect was prompt when it was possible to raise the calcium content of the blood by 15 mg per hundred cubic centimeters. If that rise did not take place, further administration of vitamin P was necessary until the higher level of calcium was obtained.

55 Strauss, H. Ueber kombinierte Brom- und Calciumbehandlung in der urologischen Balneologie, *Ztschr f Urol* **32** 689-694 (Oct) 1938

56 Schauffler, G. C., Kanzler, R., and Schauffler, C. Management of Two Hundred and Fifty-Six Cases of Infection of the Immature Vagina, *J A M A* **112** 411-416 (Feb 4) 1939

57 Rannert, M. Die blutstillende Wirkung des Citrins (P-Vitamin), *Ztschr f Urol* **32** 630-633 (Sept) 1938

OSTEOCHONDRITIS DISSECANS OF THE HEAD OF THE FEMUR

PARTIAL IDIOPATHIC ASEPTIC NECROSIS
OF THE FEMORAL HEAD

ERNST FREUND, M.D.
LOS ANGELES

Considering the large number of reported cases of osteochondritis dissecans of the knee joint and other large joints of the body, it is surprising how few observations have been made of the same condition in the hip joint. The English and American literature as far as I could find out does not include a single observation. I have been much interested in this peculiar lesion of the hip joint since my first observation of it in 1926 and have since collected 5 more cases of what is either osteochondritis dissecans or a condition closely related to it. There is no doubt that the disease is rare, and an exact diagnosis—as simple as it appears in outstanding cases—cannot always be made from a roentgenogram, representing, as it does, only one period of the lesion's development. Practically identical roentgen pictures may be presented by essentially different processes, so that the roentgenologic diagnosis of osteochondritis dissecans may not always be correct from a pathologic standpoint. It is still questionable whether even for the most common site of osteochondritis dissecans, the knee joint, different joint bodies have the same pathologic significance and whether such a body is always the result of a dissecting process which eliminates an area of primary aseptic necrosis from the living surroundings. The histologic picture of a joint body deriving from a supposedly typical process of osteochondritis dissecans is frequently so complex, as far as osseous structure is concerned, that the sequestration of a primary necrotic body can be ruled out even if at the time of surgical removal the entire body should show aseptic necrosis. Only a long-lasting process of reorganization of this area of epiphyseal bone, with simultaneous or alternating periods of bone absorption and bone apposition can explain the complicated osseous structure. Often it seems that a rather advanced even accomplished stage of revitalization has become interrupted or annihilated by a secondary trauma, which may cause complete aseptic necrosis.

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Such a body should not be likened to a sequestrum caused by osteomyelitis or tuberculosis. The pathologic process from which it originates is in many instances more complicated, there seems to be a more intrinsic disturbance than simple dissection of a necrotic piece of bone. Occasionally a careful roentgenologic follow-up over a long period leads to pictures which are incompatible with the diagnosis of osteochondritis dissecans in the sense Koenig's term has received through Axhausen's investigations, although the final picture may have all the characteristic appearances of such a lesion.

I have searched the literature for observations of osteochondritis dissecans of the hip joint and have collected the following reports. Most of them are clinical and roentgenologic reports. Few authors have reported more than a single case, which indicates the rarity of the condition. The German and French literatures present the most contributions. Owing to external reasons, my review of the literature is not complete. It seems however, to cover all the essential facts and symptoms associated with osteochondritis dissecans of the hip joint, so that I can here present a rather complete pathologic and clinical picture of this rare condition, based on the reports in the literature and on my own observations.

The following cases have been collected from the literature. The first 2 were observed by Lange¹ in 1929.

A 17 year old youth complained of increasing pain in the region of the right hip for three months. Roentgenograms revealed a typical picture of osteochondritis dissecans in the lateral quadrant of each femoral head. There were also some anomalies of ossification in the spinal column and in the left tibial tubercle.

A 22 year old man had pain in the left hip joint, gradually increasing during the last six years. Roentgenograms revealed a typical picture of osteochondritis dissecans in the left femoral head. The right hip seemed to be normal. Examination eight years later showed that the patient was practically without complaints, he walked for about two hours without difficulty but could not do more. The right hip was without subjective symptoms. A roentgenogram of the left hip showed that substitution of the necrotic subchondral area had occurred, with firm union. The osseous structure was irregular, denser areas alternating with more porotic ones. The joint surface was uneven. The joint space was narrowed, and beginning hypertrophic arthritic changes were present. A roentgenogram of the right hip showed the typical picture of osteochondritis dissecans in the upper quadrant of the head of the femur.

Lange mentioned that the first case was also observed by Haensch in 1925.

A 24 year old man had been perfectly well up to two months before observation by Bergmann² in 1929. Without trauma, there was an acute onset of pain in the left knee joint, gradually increasing and finally localizing in the left hip.

¹ Lange, M. *Ztschr f orthop Chir* 51 269, 1929

² Bergmann, E. *Deutsche Ztschr f Chir* 217 400, 1929

Physical therapy produced no improvement. The lower part of the left extremity was kept in flexion, abduction and external rotation, and there was marked restriction of motion. All attempts at motion were painful, especially weight bearing. There was a decided limp.

A roentgenogram revealed a free calcified joint body with a sharply outlined bed in the head of the femur. There were no other signs of pathologic change. There was good configuration of the femoral head.

Operation was performed, with removal of a cartilaginous bony body the size of a peach stone. The body derived from the foveal region and still had a portion of the ligamentum teres attached.

The patient made a complete recovery. Normal motion of the hip joint was present eight weeks after the operation.

The histologic picture was that of aseptic necrosis of bone. The cartilage on the surface was alive to the greatest extent. The subchondral bone marrow was active, and there was enchondral ossification of the cartilage. Further down the bone marrow and the spongy bone were alive, and the latter had a mosaic structure. The lower surface of the body, where the separation took place, showed necrotic old lamellar bone tissue.

Bergmann concluded from the activity of bone resorption and bone apposition that the process was of much longer duration than the clinical history would suggest.

A 16 year old boy had pain in the region of the left knee for six months before he was examined by Gold³ in 1930. Physical examination showed the patient to be well built and in good general condition. The left hip showed slight limitation of abduction and hyperextension. The roentgenograms showed a subchondral segment in the cranial epiphyseal pole, separated by a narrow zone of osteoporosis. The bony structure of the body was slightly cloudy with some osteosclerosis in the neighborhood. The same picture was presented by the right hip joint.

Gold observed the case for two years. Roentgenologically there was slow progress in both hip joints. The right side remained free from clinical symptoms.

Gold³ also reported the case of a 13 year old boy who complained of pain in the left hip joint for one and one-half years. The roentgenograms showed a troughlike decalcification of the upper pole of the head of the left femur, with definite condensation at the floor of the apparent depression. Within the troughlike subchondral area was a small isolated bony focus of decreased density. The joint space was of normal width. Nine months later the head was in reconstruction the troughlike impression was shallower its bony structure spotty and the bony outline of the head in reappearance the sclerotic zone or demarcation was narrower and darker. Four years later there were normal clinical and roentgenologic findings.

A 26 year old man had had pain in the left hip joint for four years preceding examination by Goldau⁴. The onset was gradual. No trauma had occurred. The pain rapidly became unbearable. On clinical examination the motion of the hip joint was free but painful. There was no muscle atrophy and only a slight limp. The roentgenogram showed an elliptic irregularity in the upper pole of the head of the femur. The right hip was normal. A plaster cast was applied for six months with some relief. Five weeks after the cast was removed the pain

3 Gold E. *Deutsche Ztschr f. Chir.* **225** 206 1930

4 Goldau D. *J. de radiol. et electrol.* **15** 567 1931

was just the same as before. The patient was considered a malingerer and under the pretext of an arthrotomy only the skin was incised. There was no improvement.

An interesting case has been reported by Støren⁵

The patient was a 27 year old man. At the age of 10, without trauma, pain appeared in the left knee, but only on motion. At the age of 14 there was swelling in the finger joints. Two months previous to admission there was a sudden onset of pain in the right knee, with articular effusion. The joints never locked. On physical examination the patient was found to be well developed, but the lower extremities when compared with the upper part of the body appeared a little thin. There was a lump to the right. A roentgenogram of the right hip joint showed at the weight-bearing portion of the femoral head a 1 to 3 cm cavity filled by a sclerotic body which was separated from the other epiphysis. Below the mousebed there was a cystic area of osteoporosis about the size of a pea. A roentgenogram of the left hip joint showed that the head of the femur was smaller and the joint space narrowed. At the weight-bearing area there was a deep defect in the joint surface, of the size of a Spanish nut, with sclerosed wall. The right knee joint showed a cavity 2 cm wide in the central portion of the joint surface of the inner condyle. In the cavity there was an irregular sclerotic body. The lateral condyle showed a small bony body close to the joint surface. The medial condyle of the left knee joint revealed an area of osteoporosis the size of a bean in the joint surface, surrounded by osteosclerosis. Examination of the hands showed separation of the ulnar portion of the head of the first phalanx of the little finger on each hand as in osteochondritis dissecans. The phalanges of the outer fingers were shorter than those of the inner ones. Some of the finger joints were uneven as in arthritis deformans.

Operation was performed, with removal of a free body from the right knee joint. There was a typical osteochondritis bed in the inner condyle. Another cartilaginous-bony body, measuring 2.5 by 1.5 by 1 cm, was observed in the lateral condyle. The patient made a good recovery.

It is interesting to note that similar articular lesions were found in other members of the family. There were ten brothers and sisters. The oldest brother had a lump since he started to walk (he probably had congenital dislocation of the hip joints), but at the age of 14 he clinically had an articular condition similar to that of Goldau's patient⁴. Another brother at the age of 10 had the same trouble in the hips. He was operated on in America for a free joint body in the knee joint. A sister had similar trouble in the hip and knee joints, clinical symptoms started relatively late, at the age 30. The other brothers and sisters were normal. The father was 60 years of age, at the age of 7 or 8, without pain or swelling, his right hip and ankle and wrist joints became stiff. He was unable to move around and had to sit in a wheel chair until the age of 10 or 11. Then the stiffness gradually subsided, and at the age of 14 he became apprentice to a tailor. There was a steady improvement, and at the age of 30 he was so well that no one could notice any disability, but there was almost always some pain in the right ankle, later the right wrist joint became stiff but was not painful. At the age of 50 there was pain in the left hip joint, with limitation of motion. On physical examination (roentgenograms were not taken) adduction flexion contracture of both hip joints was found, with marked limitation of motion. In most of the other joints there were arthritic changes with crepitation but no

⁵ Støren, H. *Acta chir Scandinav* 74 491, 1934

pain. The hands showed the same deformities as did those of his son, the patient in the present case. The fingers were short and clumsy, with abnormally short distal phalanges. There was radial deviation in the middle joint of the little fingers.

Storen concluded that there was a multiple joint lesion in the sense of osteochondritis dissecans which existed in the father and four children. Osteochondritis dissecans develops on the basis of a primary constitutional and hereditary abnormal condition or lesion. That it is so frequently isolated, occurring only in one joint, might be explained with the assumption that the primary lesion remains latent. Trauma is usually absent in the history.

Storen also mentioned 2 cases in which the condition was treated surgically and reported by Moulouguet in 1932.

A 48 year old man complained of pain in the right hip and an increasing limp during the last year before he was examined by Mouchet⁶ in 1935. The gait was good for several months, but there was vague pain, first in the region of the knee joint, then in the hip. On physical examination, right hip in adduction, atrophy of the right lower extremity was noted. Abduction and external rotation were almost nil, flexion was good. Internal rotation and circumduction were very limited. Tenderness was present over the head of the femur. The left hip (of which the patient never complained) had considerable limitation of abduction and slight limitation of external rotation. A roentgenogram of the right hip showed a large portion of the bony epiphysis separated by a semicircular zone of osteoporosis. The entire head was flattened and slightly pushed into the acetabulum. The left hip joint was roentgenologically normal, but clinically Mouchet suspected the beginning of the same trouble.

I shall now present my own observations and shall discuss each one individually with its specific problems. A final summarizing comment will stress the common features. My observations, with the exception of the last, have been reported in different German and American journals.

CASE 1—A 5 year old boy was observed⁷ at the Istituto Ortopedico Rizzoli, Bologna, Italy. The child was always in good health. Six weeks before admission trauma to the right hip joint had occurred and since then the parents had noticed a limp. On physical examination the boy appeared in good health. There was some atrophy of the right thigh, with tenderness over the right hip joint. Motion of the right hip joint was limited in abduction and rotation but was perfectly free on the left side. The roentgenogram showed a typical picture of rather advanced Perthes disease of the right hip. An unusual picture was presented by the left hip joint. The joint surface was uneven and wavy with an irregular subchondral area of osteoporosis. Otherwise the joint ends and the joint space were normal. The right hip was immobilized in a long hip spica cast. No special attention was paid to the left hip which was left free. Frequent roentgen examinations were made. The reorganization of the right femoral head took a satisfactory course.

6 Mouchet, A. *Presse med* 43 1483 1935

7 Freund E. *Arch f orthop u Unfall Chir* 30 57 1931

The osteoporotic changes in the head of the left femur first advanced slightly, then followed new bone formation without noticeable deformity of the weight-bearing joint surface.

The reorganization of the right femoral head was so well advanced after a period of two years that free weight bearing was permitted. The child had never complained of pain or stiffness in the left hip joint. The roentgenologic changes were merely an accidental finding during the treatment of Perthes' disease of the right hip.

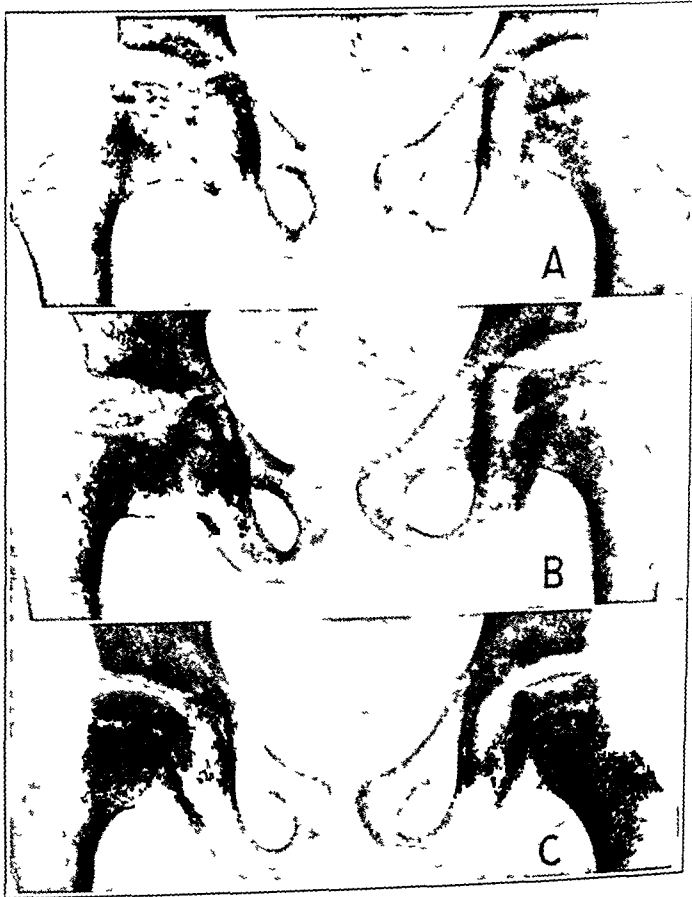


Fig 1 (case 1) —Anteroposterior view of the pelvis, taken at different periods. *A*, typical Perthes' disease of the right femur in the stage of fragmentation. This roentgenogram was taken in May 1927. Note the irregular focus of osteoporosis in the subchondral zone of the left femur. *B*, advanced reorganization of the right femur. Note the increase in osteoporosis in the left femur, with an apparent defect of the weight-bearing portion and widening of the joint space (March 1928). *C*, complete reconstruction of the right femur, with a good anatomic result. The pathologic picture of osteochondritis dissecans was observed in the left femoral head after reconstruction of the subchondral area (June 1930).

One and a half years after the boy was discharged from the hospital he returned, stating that for some time there was a little pain in the region of the left hip, with slight limitation of motion, the right hip had never bothered him, the last hip spica had been taken off.

The roentgenogram revealed a characteristic picture. Corresponding to the previously observed subchondral area of osteoporosis, a rather large lentil-shaped porotic body was present, extending over practically the entire weight-bearing portion, separated from the other normal portion of the epiphysis by a narrow translucent zone of osteoporosis. The whole epiphysis was low, but its joint surface was even when compared with the other side. There was no difference in shape. This was remarkable when one considers that the right hip suffered from Perthes' disease. A short hip spica cast was applied to the left leg for three months. After its removal there was no pain in the hip, which moved almost freely.

This case is of considerable interest. There is no doubt that, seeing only the last roentgenogram and not knowing anything about the history and previous roentgenograms, one would make the diagnosis of osteochondritis dissecans of the left hip joint because of the fact that a lentil-shaped subchondral area, sharply outlined toward the joint cavity, was separated from the other, slightly denser portion of the epiphysis by a distinct dissecting zone of osteoporosis. However, knowing the development of this subchondral area, one can quite safely rule out true osteochondritis dissecans despite the fact that the last roentgenogram appears to be fairly typical of such a condition. Osteochondritis dissecans, according to Axhausen's generally accepted conception, is the separation of a more or less wedge-shaped subchondral area of aseptic necrosis. The roentgenologic expression of this process of demarcation is the appearance of a narrow porotic zone which surrounds the necrotic area of normal or increased osseous density. The roentgenologic shadow may become "loosened up" once the reorganizing fibrous bone marrow has invaded the necrotic body.

If this is the meaning of the term "osteochondritis dissecans," such a condition cannot exist in a case in which from a roentgenologic point of view the first and safest sign—the zone of demarcation—appeared many years after the onset of the epiphyseal changes. It became visible after new osseous tissue had formed in the affected subchondral area where only bone resorption took place at first. *It was not that a primary necrotic subchondral area of old spongy bone underwent dissection, but that a reorganized portion of the epiphysis with new spongiosa did not find consolidation with its surroundings.* The linear zone of osteoporosis, therefore, cannot be considered as a zone of demarcation, it is rather a zone of pseudoarthrosis which probably formed under the influence of mechanical irritation of the subchondral area during the process of reorganization.

It is probable that while the right femur showed complete necrosis of the upper part of the epiphysis under the picture of Perthes' disease, the left femoral head was only partially affected, evidently only the subchondral area of the weight-bearing portion becoming necrotic. It is peculiar, however, that (to judge from the roentgenograms) revitaliza-

tion started immediately under the joint cartilage and gradually descended. As a rule, one expects progress in the other direction. The reorganizing bone marrow invades the necrotic area in a centrifugal direction, the marrow spaces below the joint cartilage are reached last. It may be that in this case the direction was reversed because the new bone marrow derived from the connective tissue and vessels of the ligamentum teres and not from the marrow spaces. Inasmuch as the bone-absorbing process of reorganization takes place in the centripetal direction, it is clear that the first foci of new bone formation will appear immediately under the joint cartilage, where the old necrotic bone has been removed first, and it is further clear that the new osseous foci will be surrounded at their under surfaces by the fibrous bone marrow in which they develop and which is still maintaining the process of revitalization. The whole process takes place under almost normal use of the joint, possibly even under overuse because of the protracted immobilization of the right hip in a plaster of paris cast. Intermittent weight bearing must lead to a more or less springlike up and down motion of the upper epiphysial pole, which has been deprived of its solid connection with the rest of the epiphysis. The new osseous tissue, reunited with the joint cartilage, is pressed into the underlying fibrous tissue, which under this rhythmic irritation by pressure gradually presents the symptoms of pseudoarthrosis.

It should be emphasized that it is merely by chance that physicians have the possibility of definitely ruling out osteochondritis dissecans. The earliest change in the left hip, in the case just described, would never have been detected if it had not been for the condition of the right hip joint, which was affected by Perthes' disease. There were no subjective symptoms or objective clinical findings which would have indicated taking a roentgenogram of the left hip joint. Pain and subjectively noticed limitation of motion of the left hip (some restriction of flexion and rotation had been found temporarily on previous occasions) did not appear until three years after the first observation. (The right hip joint had, meanwhile, completely reorganized, with an excellent anatomic and functional result.) This means that clinical indication for taking a roentgenogram of the left hip joint did not exist before the entire process in the epiphysis—from a pathologic standpoint—had come to a standstill and had assumed in its healing stage the picture of osteochondritis dissecans.

This is very important, because by these accidental findings a new light is thrown on the problem of osteochondritis dissecans. It is possible that a patient with an apparently typical roentgen picture of osteochondritis dissecans and with subjective symptoms of short duration has had pathologic changes in the epiphysis for many years. Such epiphyseal changes may decidedly suggest osteochondritis dissecans by their roent-

genologic appearance and may still not be those of a simple process of dissection and sequestration. This fact may explain why in so many cases osteochondritis dissecans often has such surprisingly long clinical duration, the condition is frequently present for many years without either the formation of a free body or complete reorganization. It is likely that in such cases the condition is not dissection or revitalization of an area of aseptic necrosis. Both processes—dissection or substitution—should be terminated sooner if one considers the relatively short period of two to three years it takes to reorganize completely the entire head of the femur in cases of Perthes' disease. It is, rather, a living, subchondral portion of the epiphysis, resulting from reorganization of aseptic necrosis, which has never become reunited with the rest of the epiphysis. I feel that in such cases the term "pseudo-osteochondritis dissecans" is more appropriate than "osteochondritis dissecans." It seems that a number of cases reported in the literature belong to this group, certainly the second case of Gold, in which "dissection" never occurred but in which the patient made a complete recovery with restitution of the shape and structure of the femoral head. Lange's cases are also suggestive of pseudo-osteochondritis dissecans because of the osteoporotic shadow of the dissected bodies. A true osteochondritic body has either normal or increased osseous density. The dissection prevents all porotic changes which could take place on the necrotic spongiosa. Osteoporosis is always a sign of vascularization of bone marrow. If a subchondral body has a lighter shadow than the normal surrounding bone, it must have a blood supply and cannot be necrotic. If it is not necrotic it is not a true osteochondritic body.

There is another question to be answered. If Gold's second case and my observation represent essentially the same type of pathologic process, why did the condition in Gold's patient progress to complete cure and the condition in mine to nonunion? The answer probably lies in the fact of immobilization. Gold employed immobilization for seven months, apparently a sufficient period to establish good consolidation and perfect reorganization. My patient was permitted to use and possibly even to overuse the left leg during the period of most active structural changes in the femoral head. This difference in treatment may account for the different outcome. Rigid immobilization appears natural in cases of bone grafting to bridge joints or fractures and essentially the taking of a bone graft is nothing but a process of reorganization of aseptic necrosis of bone. I was able to demonstrate in 1931 that early adequate protracted immobilization gives better results in cases of Perthes disease than late immobilization or none at all. If it were not for secondary complicating traumatic factors occurring during the active stage of reorganization aseptic necrosis of bone should always heal with complete restitution. To avoid secondary trauma immobilization is of

greatest importance. It is the treatment of choice if only the correct diagnosis of aseptic necrosis could be made on time. The latter, however, will remain a *primum desiderium*. Clinical symptoms are usually expressive of late complications, of deformity or of direct articular involvement. Roentgenologic recognition of aseptic necrosis of bone is possible only when reactive changes, either osteoporotic or sclerotic, have taken place in the living tissues in the region which also indicate a late stage of the disease. One seldom is able, therefore, to observe a case of correctly diagnosed idiopathic aseptic necrosis of bone in an early stage and a complete restitution of form and structure, to be expected *a priori*, will thus unfortunately never take place.

CASE 2—A 15 year old boy was observed⁸ at the Istituto Ortopedico Rizzoli. A limp appeared at the age of 13, immediately after the boy had had diphtheria. The pain was mild except after walking for a great distance. For the last few months the limp had been more marked, but the pain remained mild.

On physical examination the boy was observed to be decidedly hypoplastic. His body resembled that of a boy of 11. There was a strong disproportion between the length of the trunk and that of the extremities, in favor of the latter. In upright position the pelvis was inclined to the left. The right lower extremity was kept slightly abducted and externally rotated. The knee was slightly flexed. The left leg was adducted. There was convex lumbar lordosis on the left side. There was a decided limp, with a list of the trunk to the right. The Trendelenburg sign was absent. The extremities were of even length. The right hip joint showed slight abduction contracture, there was no adduction or external rotation. No pain or tenderness was present. The left hip joint had free motion. A clinical diagnosis of Perthes' disease of the right hip joint was made.

Roentgen examination showed both femoral epiphyses to be symmetric. The upper pole of each was porotic. It was separated from the other, normal portion of the epiphysis by a zone of osteosclerosis which was widest in the middle and thinner toward the joint surface. The subchondral focus of osteoporosis was a little larger in the left femur, where the zone of osteosclerosis was also much stronger and reached down to the epiphysal plate. The capital epiphyses were low and slightly flattened over the porotic area. The joint space was somewhat widened. The bony structure of the subchondral area in the right hip was different from that in the left. The spongiosa was still connected with the joint cartilage in the right femur, it was denser than the portion close to the sclerotic zone of demarcation. In the left femoral head there was more fanlike dissolution of the focus, with rather regular alternation of markedly porotic with less porotic strips.

The condition in this case was apparently intimately related to "pseudo-osteochondritis dissecans" inasmuch as a porotic subchondral portion, evidently in the middle of an active process of reorganization, was separated by a distinct zone of demarcation from the rest of the epiphysis. In this instance, however, it was not a separation by dissection, the subchondral focus was surrounded not by a zone of porosis but by marked osteosclerosis.

⁸ Freund, E. Fortschr. a. d. Geb. d. Röntgenstrahlen 41: 935, 1930.

Exactly the same type of case with the same roentgen picture has been described by Kreuz⁹ as "unusual changes in the upper femoral epiphysis" Kreuz's patient was a 9 year old girl who for two years limped and kept the right leg in external rotation Clinically, as in my case, the diagnosis of Perthes' disease was made, but roentgenologically there was a troughlike defect in the upper pole of the epiphysis, separated from the normal portions of the epiphysis by a strong band of osteosclerosis

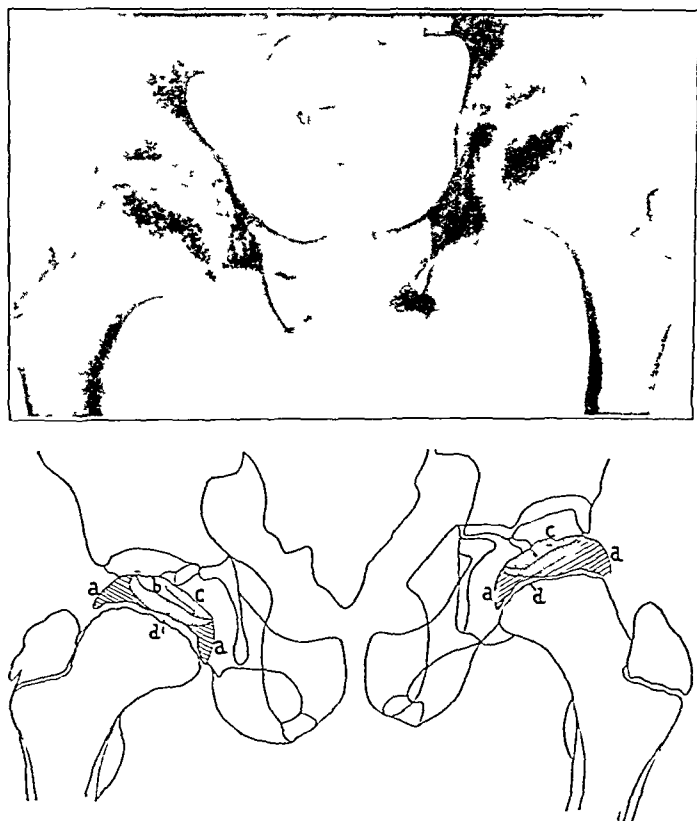


Fig 2 (case 2)—Anteroposterior view of the pelvis, with corresponding sketch There is a peculiar lesion of both hip joints, resembling osteochondritis dissecans *a*, normal portion of the epiphysis *b*, complete absorption, *c*, marked osteoporosis in the subchondral area, which is surrounded by a zone of osteosclerosis *d*

Kreuz correctly ruled out Perthes' disease because there never was a case of Perthes' disease starting from a circumscribed focus of osteoporosis within the capital epiphysis He also rejected osteochondritis

⁹ Kreuz L Fortschr a. d. Geb d. Röntgenstrahlen 40 1034 1929

dissecans, because during the whole time of observation there was no shadow of a sequestered osseous body, on the contrary, it seemed that the subchondral focus of osteoporosis enlarged during the period of observation. He considered his case as a special form in the group of osteochondropathies.

Although it is true that in Kreuz's case and in mine the conditions observed were neither Perthes' disease nor osteochondritis dissecans they were closely related to both. There is no essential difference among these forms. They all are primarily aseptic necrosis of the femoral head. The differences derive from the extension of necrosis and from the later complications of the process of reorganization. In Perthes' disease it is the entire bony epiphysis which becomes necrotic, in Kreuz's case and in mine, and in true cases of osteochondritis dissecans, it is only the subchondral portion of the epiphysis.

It is the degree of involvement of the epiphysis which differentiates these conditions from Perthes' disease, it is the difference in the process of reorganization which separates them from true osteochondritis dissecans. There are essentially two courses the process of reorganization may follow in a case of aseptic necrosis: reorganization in the form of slow substitution of the necrotic tissue by living bone marrow or demarcation (sequestration). The latter, as I shall point out, seems always to be a late complication, it follows a process of substitution at a rather advanced stage, especially if reorganization is hindered secondarily by traumatic factors. In the case of Kreuz and in my case 2 the process of reorganization followed the first modus. The focus of subchondral necrosis became resorbed and slowly replaced without leading to much deformity. Up to this point it had behaved in exactly the same way as does pseudoosteochondritis dissecans. The only difference was in the zone of demarcation, in pseudo-osteochondritis dissecans the zone of demarcation is osteoporotic, in Kreuz's case and in my case it was osteosclerotic. I have explained the osteoporotic zone, considering it as pseudoarthrosis. The explanation of the sclerotic zone of demarcation is as follows: The necrotic subchondral area undergoes revitalization in a centrifugal direction, the bony tissues close to the joint cartilage are the last rests to be resorbed and replaced. The zone of sclerosis is, as I shall show by the histologic picture in the following case, primarily a zone of reaction. This reaction is probably due to stimulation of the living bone marrow to osteogenesis by toxic products from the decomposition of the necrotic marrow. Primarily it is of no static importance. Later, however, if necrotic spongy bone is resorbed and the mechanical firmness of the epiphysis is weakened, the central portion of the epiphysis will be exposed to further mechanical irritation which will result in bone apposition and sclerosis. This is essentially the mechanism observed in cases of hypertrophic arthritis, in which the

superficial spongy bone close to the joint surface is fortified by apposition of new bone as an expression of the increased mechanico-static demands of this denuded articular area

The following case has not been studied carefully from a clinical standpoint. The bilateral lesion of the hip was unrecognized during life, and no roentgenogram was taken. The patient died in a charitable institution in Vienna, and it was the postmortem examination which disclosed the peculiar lesion of both hip joints.

CASE 3—A 77 year old woman was observed at autopsy.¹⁰ The clinical history was poor. The patient was supposed to have fallen two years before death. She had been unable to get up because of sudden severe pains in both hip joints. The pain was associated with frequent muscle spasms in the lower extremities. There was some gradual improvement, but she had remained bedridden since the day of the fall. Both knee and hip joints were restricted in motion, and there was spastic flexion contraction of the knees and hips. (Encephalomalacic areas were observed in the basal ganglia and the inner capsule. The autopsy did not reveal a fracture of the neck of the femur, which had been suspected clinically, however, there were interesting findings in both hip joints, which I consider it worth while to discuss in more detail.

The head of the right femur looked as though it had been flattened, impressed and made smaller by pressure from above. The joint cartilage was preserved, it was even smooth and free from arthritic changes except where the joint surface was flattened, there it showed three folds, as though by resorption of the underlying bone the cartilaginous cover had become too large and for this reason had become folded. Over the posterior aspect of the head the joint cartilage was eroded and even absent over a larger area, as a sign that a large area of the joint surface was out of contact with the acetabulum, owing to the ankylosis. There were also a few fibrous adhesions.

A surprising picture was presented by the cut surface. The femoral neck was normal, but the head had disappeared to a great extent, it showed, nevertheless, a fairly well preserved cartilaginous cover. The diminution in size of the head was caused by necrosis of a large subchondral portion of the epiphysis, which had already undergone extensive resorption. The rest of the necrotic area was still present below the cartilage yellow and dense like caries necrotica. A wide zone of hyperemic fibrous tissue was present between the necrotic and the normal spongy bone. Included in the fibrous tissue was bluish transparent cartilage which differed considerably from the old yellow opaque joint cartilage. The spongy bone of the femoral neck showed some signs of sclerosis just under the fibrous zone of demarcation.

To explain the disappearance of the head of the femur and the pleat formation of the joint cartilage, it should be mentioned that a fracture line was running through the necrotic spongy bone immediately below the joint cartilage. Thus two factors were responsible for the loss of spongiosa: (a) absorption by fibrous tissue along the zone of demarcation and (b) friction of the osseous surfaces along the fracture space. The spongy bone was ground to detritus. The fracture space, however, because of the intra-articular pressure remained capillary and all the detritus was pressed into the narrow spaces.

10 Freund, E. Virchows Arch f path Anat 261:287 1926

The head of the left femur was not as much deformed and not quite as small as that of the right. The deformation was not on the upper but more on the medial surface, at the site of the fovea capitis. The joint cartilage as a whole was well preserved, but in this also folds were present, which, if the joint was observed from the surface, remained almost unnoticed because fibrous tissue had filled the valley between the cartilaginous folds. The posterior surface revealed an extensive area of cartilage absorption exactly like that in the right hip joint.

The cut surface resembled that of the right femoral head. Only the localization of the area of necrosis was different. The yellow color and the density of the necrotic spongiosa were suggestive of tuberculous caries, but the absence of erosion of the cartilage easily ruled out tuberculosis. The cut surface also revealed



Fig 3 (case 3) —Frontal sections through the right femoral head compared with sections of a normal joint, to illustrate the loss of osseous substance from the epiphysis through subchondral aseptic necrosis. The dotted line indicates the borderline between the head and the neck of the femur. The joint cartilage is fairly well preserved but is very irregular over the depressed area.

that the head was considerably smaller than normal. Tracing a circle with the radius of the normal joint margin, one realized that the necrotic area was decidedly displaced inward and that the gradual resorption of necrotic spongiosa had led to the fold formations of the joint cartilage.

Both femoral heads were cut in slices, and numerous sections were studied histologically. I refrain from giving a detailed histologic report, which has been published elsewhere,¹⁰ and offer here a brief summary which will help in the understanding of this peculiar disease.

A subchondral portion of the epiphysis had undergone aseptic necrosis of the spongiosa and bone marrow. The necrotic focus of the left femoral head was considerably larger than that of the right. A fracture line of intravital origin passed through the necrotic bone close to the joint cartilage. There was no sign of callous formation, because the fracture ran through necrotic bone entirely, far away from living bone marrow. Constant friction of the fracture surfaces ground up the necrotic bony trabeculae near the fracture space to a fine powder which filled the fracture space as well as marrow spaces. On the other hand, the loss of subchondral bone deprived the joint cartilage of its solid support, and it showed some deep implications, leading in some places to complete and multiple fractures.

The spongiosa of the head of the femur at the border between the necrotic and the living bone marrow still showed continuity in some places, and in others there was complete separation by a zone of fibrous tissue. There were no stages of dissection between these extremes. The separation occurred within the area of necrotic osseous tissue which in part remained included within the fibrous zone of dissection.

Where the bony trabeculae passed without interruption from the focus of subchondral necrosis into the living central portion of the epiphysis, a gradual replacement of the necrotic bone marrow by fibrous marrow took place, and soon afterward an apposition of primitive dark blue fibrous bone occurred along the surfaces of the necrotic trabeculae. The necrotic spongiosa extended quite far into the living fatty marrow below the fibrous marrow spaces. The trabeculae within the necrotic area, deprived of all immediate possibilities of resorption, had preserved the same thickness as they had the day they were effected by aseptic necrosis, while the spongiosa in living fat marrow showed considerable signs of atrophy from inactivity. The subchondral necrotic bone, dense and free from all resorption, gave a dark shadow in the roentgenogram, thus contrasting sequestrum-like with the porotic surroundings. Contributory to this relative density was the accumulation of calcified detritic material of ground-up bony trabeculae and calcified joint cartilage in the necrotic narrow spaces.

Where sequestration of the necrotic bone has occurred, the picture was different. A wide zone of dense hyperemic fibrous tissue interrupted the continuity of the necrotic spongiosa. Necrotic trabeculae were found above and below the fibrous zone of demarcation, but not within it. The trabeculae below the fibrous tissue again showed the dark blue endosteal layers of primitive fibrous bone which even extended over living trabeculae. Thus resulted a zone of osteosclerosis immediately below the dissecting fibrous tissue. The osteosclerosis could be considered in part as due to toxic irritation of bone marrow (through the resorption of toxic products from the decomposition of necrotic bone marrow) in part, however, it was the expression of increased mechanical irritation, the subchondral necrotic area with every movement of the joint being pressed against living spongiosa. The dissection through the necrotic bone took place typically by lacunar resorption along the fibrous zone of demarcation.

This revealed clearly that the process of reorganization may be different in different areas. The necrotic bone marrow may become replaced by fibrous tissue and new bone may be laid down on the surfaces of old osseous trabeculae. The other form also leads to substitution of necrotic bone marrow by fibrous tissue, but at the same time resorption of the necrotic trabeculae takes place, with sequestration of the necrotic bone. The first form may be called organization, the

second sequestration of the area of aseptic necrosis. The reason for this difference in the process of reorganization is not always clear, mechanical factors, shearing stresses or ultra-physiologic pressure may be of importance. A better understanding of these factors would be of great help in prognosticating whether in a certain case of aseptic necrosis osteochondritis dissecans will occur. It seems that the size of the focus of necrosis is of greatest importance. A large focus which includes most of the epiphysis will hardly ever become sequestered. Dissection may take place at a later stage of reorganization, when the necrotic bone is reduced to a relatively small subchondral portion. The mechanical irritation of this region apparently has a decisive influence on the process of reorganization. Therefore it is more likely that a dissecting process will be an early response to aseptic necrosis if the latter involves only a smaller subchondral portion of the epiphysis. It will not be observed at an early stage of reorganization if the necrosis is extensive and involves the greater part of the epiphysis. In such cases, dissection or sequestration will be a late complication, caused by mechanical irritation of the zone of organization as soon as the latter reaches the subchondral area and the danger zones there.

The anatomic study of this case furnishes the key to the full understanding of aseptic necrosis of bone and the different forms of reorganization. Although not an outstanding instance of osteochondritis dissecans, it shows better than a true case could that osteochondritis dissecans is only a form of reorganization which may but does not necessarily follow the occurrence of bone necrosis.

Certainly the age is most unusual in this case. Physicians are accustomed to finding aseptic necrosis in childhood or adolescence. In old persons it may occur as a result of severe trauma, for instance, following fracture of the neck of the femur, partial or complete necrosis of the proximal fragment may occur, in its idiopathic form, however, which may lead to osteochondritis dissecans, it has never to my knowledge been observed in a person of such old age as the patient in case 3. One might think, in view of the poor clinical history in this case, that the aseptic necrosis of both femoral heads had been of many years' duration. One cannot rule out the possibility that it started in the prime of life and lasted several decades without coming to full organization. The fall two years before death, mentioned in the history, certainly could not be responsible for the lesions in both femoral heads, which from a pathologic standpoint suggested a difference in duration. (This seems to be the rule in cases of bilateral osteochondritis dissecans: roentgenologically the condition is almost always more advanced on one side than on the other. One side may present clinical symptoms while the other is clinically normal despite considerable roentgenologic changes.) There is as yet no way to determine the duration of a true

of aseptic necrosis, but it usually is much older than the clinical history would lead one to believe. If idiopathic aseptic necrosis should really be a disease of young persons exclusively, case 3 would show that the condition may be present for decades, with disablement delayed until the last two years of life. However, one cannot rely too much on this argument. It is altogether hypothetical, so little being known of the case history. I can say only that the definite trauma two years before death must have acted on bone tissue already pathologic, it could have been responsible for the subchondral fracture through the necrotic bone and for a sudden arthritic reaction.

Case 3 has a great resemblance to cases 4 and 6, in which the patients were robust males who showed essentially the same clinical and roentgenologic symptoms and the same underlying pathologic condition.

CASE 4—This case was observed¹¹ in the orthopedic department of the University of Iowa. A 45 year old man complained of pain and stiffness of the right hip. Two years before admission while he was carrying one end of a long plank, he slipped on wet ground and was knocked down backward. The plank struck him over the right hip anteriorly. There was immediate pain around the right hip. He walked with difficulty, and his superintendent assigned him a lighter job for the remainder of the day. Roentgenograms were not taken, but heat therapy was advised. There was great improvement, but the pain did not disappear completely. He returned to work in two weeks. After four or five weeks he had to stop working again because of pain in the hip and a limp. He was then in bed four or five months. During the winter months, especially pain and stiffness in the hip joint were severe. About six months before admission the hip became almost completely rigid, and since that time he had been unable to put on his right shoe. At the time of his admission to the clinic, pain was less marked, and for the last year changes in the weather had had little effect. The patient had lost 20 pounds (9.1 Kg.) since the accident.

On physical examination he was seen to be a well developed, powerfully built man who walked with a marked limp on the right side. The right lower extremity was held in about 25 degrees external rotation, 15 degrees abduction and 10 degrees flexion, only 10 degrees of flexion was possible. There was slight tenderness over the anterior aspect of the hip. There was no atrophy of the thigh.

The patient was admitted for physical therapy elsewhere, under which he improved considerably. The pain disappeared almost completely, and there was increase of motion (flexion from 165 to 120 degrees). He was then discharged to continue with heat treatment at home. He returned again after one year. There was no improvement, the hip was practically rigid, showing marked flexion-abduction and external rotation contracture.

Roentgenograms were taken at different intervals (the earliest six months after the accident). They always showed more or less the same rather unusual picture. The head of each femur contained a dark shadow. In the left femur the shadow was wedged shaped. The base of the wedge comprised almost the entire joint surface. The point was in the center of the neck. In the right femur the sclerotic area involved the subchondral region but the other part of the head showed irregular bony trabeculation. Through the upper part of the head

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of the femur, opposite the roof of the acetabulum, extended an irregular fracture line, more or less parallel to the joint surface, separating a slightly flattened lentil-shaped fragment from the other portion of the femoral head. Where the fracture line ended at the joint surface, a small spicule of bone protruded into the joint cavity. The joint cavity was of normal width and the joint surfaces were smooth, except that beginning formation of marginal exostoses could be seen on the inferior part of the ilium, on the right side.

From the clinical and roentgenologic findings, the diagnosis of degenerative (hypertrophic) arthritis of the hip joint was made. It was thought that the condition probably had developed on the basis of an intra-articular fracture of the head of the femur. The dark shadow of the femoral epiphysis was unusual for hypertrophic arthritis but was considered as representing a pronounced degree of reactive osteosclerosis in the subchondral zone.

Because there was practically no improvement despite protracted physical therapy, an exploratory operation, followed possibly by an arthroplasty, seemed indicated.



Fig 4 (case 4) —Anteroposterior view of both hip joints. The dark shadow in the epiphysis represents an area of aseptic necrosis, wedge-shaped in the left femur without deformity of the head. There is a subchondral irregular fracture line through the subchondral zone of the weight-bearing portion of the right femur, with a small spicule of bone, deriving from the subchondral bony lamina and pointing into the joint cavity. The resorptive changes of the necrotic bone are more advanced in the right femur. There is deformity of the femoral head, consisting of a depression of the upper pole and beginning hypertrophic arthritic changes at the joint margins.

Operation was performed, the right hip joint being exposed between the tensor fasciae latae and the gluteus medius muscles. The joint capsule was considerably thickened. It was incised, and the head of the femur was dislocated into the wound. It was markedly deformed, it was enlarged and showed a cartilaginous cover with pronounced degenerative changes and unevenness. The ligamentum teres was still present, and there were marginal exostoses around the entire joint surface. Eroded areas of the joint cartilage were relatively scarce. The head of the femur was trimmed to reduce its size, and a very unusual picture was encountered. For the greater part the head of the femur was necrotic. The

spongy bone was dense, yellow and not bleeding. The yellow necrotic areas were surrounded by hyperemic, more porotic portions which were separated from the necrotic bone by a sharp line of demarcation. Almost all of the necrotic bone was removed, together with the joint cartilage. The divided head was covered with a flap of fascia lata which was also sutured to the joint capsule. The head was reduced and the capsule closed.

The findings at operation clearly explained the roentgenologic picture. The dark shadow represented an area of aseptic necrosis of the epiphysis. Histologically the involved area presented essentially the same pictures as the areas of necrosis in case 3 except that in the latter instance the lesion was more advanced. Dissection of the necrotic tissue had started but had not yet reached such a degree as to become manifest in the roentgenogram. Therefore, one cannot call the condition osteochondritis dissecans, although it would have slowly developed into this. The condition was bilateral idiopathic aseptic necrosis of the femoral head, complicated by a subchondral fracture and articular symptoms before the process of substitution was fully changed to a process of sequestration.

The patient was followed up for two years after the operation. For more than one year he complained very much of pain and stiffness in the hip, although the objective examination showed a satisfactory result. (The lawsuit for workmen's compensation was still pending.) About eighteen months after the operation the patient himself noticed much improvement. He discarded his crutch and walked well with a cane. The muscles around the hip became stronger, and active motion was rapidly increasing. The passive range of motion was for flexion, 75 to 80 degrees, for abduction, 25 degrees, for adduction, 0, for internal rotation, 5 to 10 degrees, and for external rotation, 40 degrees. There was about 1 inch (2.5 cm.) of shortening, and atrophy of the right thigh was still marked.

Apart from the interest this case arouses from the roentgenologic and pathologic standpoints, it presents an important medicolegal aspect which frequently has to be considered in cases of this type when the patients are otherwise normal workmen in the prime of life. This case was a "compensation case." The patient claimed that his disability started with an industrial accident. A direct trauma to the hip was followed by pain and stiffness. The earliest roentgenogram was not taken until six months after the accident. Roentgenograms taken then, on several occasions, showed the conditions mentioned. It is hard to make a definite statement as to how long the aseptic necrosis was in existence, that is, whether it was half a year old or older. It probably was older, but there is no proof for this assumption, only a roentgenogram taken the day of the accident or shortly after would settle this question. Unfortunately for the patient (also from a practical standpoint) no roentgenogram had been taken immediately. However, regardless of whether the aseptic necrosis of the head of the right femur was six months old or older, it is certain that the trauma which the patient sustained could not have been responsible for the aseptic necrosis of both femoral heads. The patient never complained of the left hip which showed essentially the same picture as the right. There was only

one difference—in none of the numerous roentgenograms was there a subchondral fracture line in the left hip joint. It was present in the earliest picture in the right femoral head. It is possible—and this is the only thing which speaks in favor of the patient—that the subchondral fracture of the right femur was due to the industrial accident. The aseptic necrosis, evidently in this case “idiopathic” and without a traumatic cause, must have preceded clinical symptoms for a long time, possibly for years. The secondary subchondral fracture (a pathologic fracture because it occurred in necrotic bony tissue) was intra-articular and had certainly led to augmentation of arthritic symptoms, it may even have been responsible for the very beginning of clinical symptoms. On the other hand, it is true that epiphyseal aseptic necrosis per se may be followed by degenerative and hypertrophic arthritic changes without the occurrence of a definite secondary complicating trauma. Therefore, from a medicolegal point of view the patient has to be considered in the same light as a patient with metastatic malignant tumor or with Paget’s disease who sustains a “spontaneous” fracture of the affected bone. His claim for compensation had to be rejected, on the basis that his primary osseous disease, i. e., aseptic necrosis, was certainly not caused by the industrial accident. The subchondral fracture may have been the result of the injury, but since such a fracture develops so frequently without injury, the fracture in this case should not be attributed necessarily to the trauma. It is to be expected that symptoms similar to those present on the right side will also develop sooner or later on the left side. This will prove that the entire pathologic process in this case was essentially independent of the industrial accident. A somewhat similar problem was presented in the following case.

CASE 5—A 31 year old Negro, a butcher, complained of pain in the left hip, which came on gradually.¹¹ The only fact the patient could offer in explanation was that during his work he had to assume a certain position in which his hip tired easily. The hip became stiff but limbered up spontaneously. On physical examination, mild flexion contracture of the left hip joint with some limitation of motion was found. The results of laboratory tests were essentially negative, but roentgenograms showed an unusual picture of irregular osteoporosis in the femoral head and slight narrowing of the joint space. Physical therapy followed by immobilization in a plaster of paris cast did not afford any relief of symptoms. Biopsy of material from the head of the femur and the joint capsule was performed. A typical picture was encountered of subchondral aseptic necrosis undergoing reorganization by fibrous bone marrow. There were nonspecific chronic inflammatory changes in the joint capsule, but not to a greater extent than is expected in a case of aseptic necrosis of bone.

The follow-up disclosed increasing stiffness of the hip joint, with pain on weight bearing. A roentgenogram taken more than one year after the first showed an increase in the irregularity of the osseous structure without lead to the picture of osteochondritis dissecans. This case did not permit a definite diagnosis. It was not studied long enough. In several ways it differed from

case of aseptic necrosis. The narrowing of the joint space with marked restriction of motion suggests more a destructive articular process. A complement fixation test for gonorrhea gave a 4 plus reaction.

Mouchet⁶ stated that gonorrhea is of possible etiologic importance in cases of osteochondritis dissecans of the hip joint, but I am skeptical concerning such a connection. I reported case 5 because it has several features in common with cases of osteochondritis dissecans, but it is not sufficiently clear from a diagnostic standpoint to warrant further conclusions.

CASE 6—A 34 year old man, a painter, complained of pain in the hip and knee joints, especially of the left side. The trouble had started rather acutely with pain in the left leg one morning when he awoke about two years previously. The pain at first was in the region of the knee but later settled in the left hip. There was no direct relation to a trauma, although a short time previous to the onset



Fig 5 (case 5)—Aseptic necrosis of the head of the left femur in two different stages of reorganization. *A*, irregular osteoporosis in the epiphysis, due to reorganization of aseptic necrosis. The subchondral area is still dark. There is slight narrowing of the joint space (August 1935). *B*, reorganization of most of the head, with the bony structure still irregular. The small subchondral dark area represents the rest of the necrotic epiphysis. There are arthritic changes at the joint margins (November 1936).

of subjective symptoms the patient had had a fall from a ladder, landing flat on his back. He had had to stay in bed for two days and had been unable to work for about a week. The left leg gradually became weaker, and the motion in the left hip joint was much impaired. He tired very easily.

On physical examination he was found in good general condition. His arms and trunk were powerfully built and contrasted considerably with the lower extremities, which appeared atrophic. He walked with the use of a cane and with a decided limp to the left. There was a slight adduction contracture of the hip joint and atrophy of the left lower extremity. There was no shortening. The left hip joint showed limitation of motion, flexion from 180 to 90 degrees, external rotation of 5 degrees and all other motions absent. The right hip joint which

did not give much subjective trouble, also showed considerable restriction of motion (flexion from 180 to 75 degrees, adduction 20 degrees, abduction 25 degrees, internal rotation 0, external rotation 5 degrees) There was some tenderness over the anterior aspect of the left hip joint The Trendelenburg test was negative on the right and questionable on the left Clinical examination of the knee joints showed them to be normal

The clinical symptoms suggested a lesion affecting both hip joints, the left more than the right The subjective symptoms of pain in the knee joints could be explained as pain referred from the hips The limitation of motion in the left hip joint, with the adduction contracture and absence of more general symptoms, suggested the diagnosis of simple hypertrophic arthritis, and the restriction of motion of the right hip joint well agreed with such a diagnosis However, the age of the patient, without a history of disease of the hip joint in early childhood or in adolescence, made the clinical diagnosis of hypertrophic arthritis doubtful A direct traumatic lesion could safely be ruled out because both hip joints seemed to be affected, the left more than the right, and the one trauma mentioned in the history could not be made responsible for symptoms in both hip joints From a clinical point of view, therefore diagnosis had to be deferred

Roentgenograms were taken and revealed an unusual but characteristic picture There was considerable deformity of both femoral heads, more pronounced in the left than in the right The deformity involved mainly the weight-bearing portion, especially the upper outer pole The joint surface of the left femoral head was irregular, flattened over the lateral portion and impressed The upper part of the epiphysis appeared sequestrum-like in a very dark shadow, which toward the periphery became cloudy and seemed almost completely separated by a denser zone of osteoporosis from the rest of the epiphysis Beyond this almost bone-free zone a distinct but irregular band of sclerosis was found, which thus demarcated definitely the entire diseased area from the femoral neck Several well circumscribed, cystlike areas of osteoporosis were found in the neck, close to the zone of demarcation At the joint borders, especially opposite the outer edge of the roof of the acetabulum, hypertrophic arthritic changes were noticed in the form of marginal exostoses There was slight lateral subluxation of the head of the femur

The changes in the right hip joint were essentially the same, but they were less advanced and less extensive Here, too, the upper outer portion of the femoral epiphysis appeared in a dense shadow which became loosened from the lateral surface of the neck At this area the shadow was more cloudy, with irregular osseous structure No definite zone of demarcation was visible, although it seemed that some osteosclerotic changes had taken place at the lower surface of the dark area The joint surface over the diseased weight-bearing portion was irregular, it was broken into several pieces and was flattened and depressed The joint space of each hip joint was of normal width or even wider than normal, corresponding to the flattening deformity of the femoral head

From this characteristic picture the diagnosis of bilateral aseptic necrosis of the femoral head was made There was definite sequestration (osteochondritis dissecans) in the left femoral head, while the process of reorganization in the right hip was still aiming at gradual substitution of the necrotic area From a roentgenologic point of view the case was similar to, indeed almost identical with cases 3 and 4 Once one has become acquainted with the roentgenologic appearance in such cases, the diagnosis can be made easily (It seems that in a number

of such cases the condition is considered chronic arthritis, usually hypertrophic arthritis, as long as the existence of a zone of demarcation does not suggest the diagnosis of osteochondritis dissecans. The underlying pathologic process, the idiopathic aseptic necrosis, is apparently not taken into diagnostic consideration frequently enough. I do not doubt that with more attention and better knowledge the recognition of this peculiar condition will become easier and the number of clinical observations will grow.)

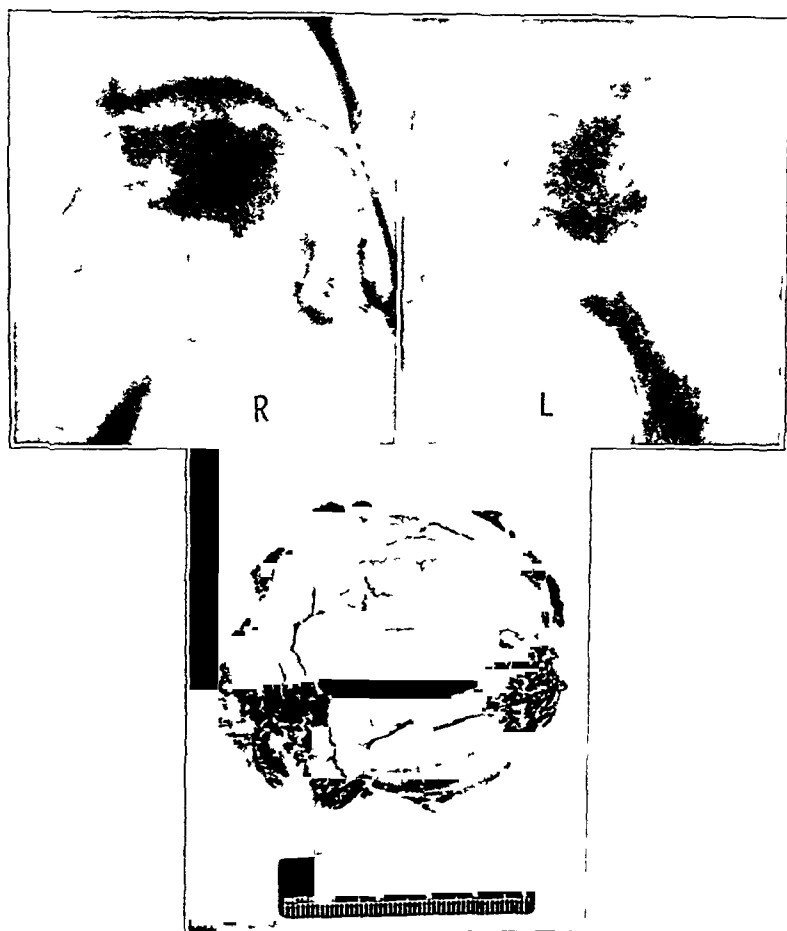


Fig. 6 (case 6) —Anteroposterior view of both hip joints and photograph of the left femoral head seen from above. Note the dark shadow of aseptic necrosis in the upper outer pole of the right femur with depression and corresponding widening of the joint space. There is beginning absorption of the necrotic area from below. More marked changes are discernible in the left femur, with the pathologic picture of osteochondritis dissecans. Note the separation of the dark necrotic epiphysis by zones of increased and decreased density. There is pronounced deformity, with depression of the necrotic area and lateral subluxation. Cystlike areas of osteoporosis are present in the neck of the femur. The photograph reveals the unevenness of the joint cartilage with its folding and perforation, its erosion around the lesser trochanter and its wreathlike marginal excrescences.

and painful period consideration should be given to immobilization in a hip spica cast to give the zone of pseudoarthrosis a chance to fill in so that firm consolidation with the epiphysis may be reestablished. I do not think that such a reorganized area will ever come to complete separation, with appearance of a free joint body. It is usually situated at the upper pole of the femoral head and is well protected by sound and thick joint cartilage.

Inasmuch as the process of reorganization does not tend to sequestration, the only mode of separation is on a traumatic basis. It is difficult, however, to conceive how trauma could lead to dehiscence of the joint cartilage around the margins of the subchondral body. The similarity of the roentgen appearance in such cases with that in cases of osteochondritis dissecans of the knee joint suggests surgical treatment. I doubt, however, that operation would be of great benefit, considering that clinical discomfort is not caused by "internal derangement" of the hip joint or by a free joint body. Surgical removal of the subchondral body with its cartilage cover would aggravate the symptoms by creating a deformity at the most important part of the joint, that is, at its weight-bearing portion.

Still the aforementioned observation of Bergmann² suggests that osteochondritis dissecans of the hip joint may lead to the formation of a free joint mouse with locking of the joint. However, Bergmann's case is different from the other cases described. The body derived from the region of the fovea capitis where, because of the thinness or lack of joint cartilage, a separation can take place much more easily than at the free weight-bearing joint surface. Although there is no doubt as to the correctness of Bergmann's diagnosis of osteochondritis dissecans, one cannot help but feel that his case is rather unusual as far as the clinical symptoms and the localization of the body are concerned. As far as I could find out, in no other case has osteochondritis dissecans of the hip joint led to a free joint mouse.

There is another form of pseudo-osteochondritis in which the line of demarcation between the subchondral area in reorganization and the rest of the epiphysis is represented by a sclerotic zone. This is shown by the experience of Kreuz⁹ and by my own experience in case 2. Here, too, mechanical factors besides a toxic stimulus to osteogenesis are probably responsible for the development of the sclerotic zone. In either form, whether it leads to a zone of pseudoarthrosis or one of osteosclerosis, the reorganization of the subchondral area takes place in centripetal direction.

The patients in this group were young. With the exception of the patient in case 1, who was still in the first decade of life, they were in the second and third decades. The osseous focus in separation was relatively small, and the prognosis seemed to be quite good. But there

is another group of cases in which the patients are adults in the fourth and fifth decades of life. Males, as those in the first group, seem to be by far more affected than females, and the patient usually is a robust type of man doing hard physical work. Very commonly, but not always, both hip joints are involved, as in Mouchet's⁶ case and in case 5, the condition being usually a little more advanced in one than in the other. A large portion of the epiphysis, for reasons which are entirely unknown, undergoes aseptic necrosis. The area of necrosis always is much more extensive than in the first group of cases, the greater part of the epiphysis and even portions of the femoral neck may be involved. Roentgenograms taken in the early stages show characteristically a wedge-shaped dark shadow, the point of the wedge being in the center of the head or neck and the base comprising the entire joint surface. The joint surface in such cases is fairly even, and motion may be almost normal. Nevertheless, even in such early roentgenologic stages the condition is considerably advanced from a pathologic point of view. When the shadow of the necrotic epiphysis appears darker than normal there must be a fracture in the subchondral area, with grinding up of necrotic bony trabeculae. The aseptic necrosis will lead to reactive changes from the side of the living bone marrow, aiming at reorganization of the necrotic head in the centrifugal direction. As long as this process of reorganization is not interfered with by mechanical factors, it will follow the way of gradual resorption of the old necrosis and substitution by new bone. This slow process is the same as that observed when large bone grafts are "taking." A great many of the necrotic trabeculae remain, they receive only sheaths of new bone. The further the process of reorganization advances toward the joint surface, the more it will become complicated by mechanical irritation. The gradual loss of bone by osteoclastic bone absorption at the lower periphery of the area of necrosis will weaken the mechanical support of the joint cartilage, which will break in or become folded to adapt itself to the decreasing osseous epiphysial substance. If joint motion and weight bearing are continued the constant mechanical irritation will change the process of gradual substitution to a process of dissection, which will separate the remaining subchondral area of necrosis from the reorganized portion of the epiphysis by a zone of firm fibrous tissue, producing osteochondritis dissecans.

It is of greatest interest and must be emphasized that the zone of dissection in true osteochondritis dissecans is a late occurrence just as it is in pseudo-osteochondritis dissecans. Dissection does not seem to be a primary response to aseptic necrosis of the epiphysis. It takes place only when the primary process of creeping replacement is interfered with by mechanical irritation and more marked trauma. The zone of dissection, therefore, never separates the entire focus of necrosis; it runs through

the necrotic area, a part of which has already undergone revitalization. On histologic examination one finds necrotic bony trabeculae above and below the dissecting fibrous tissue. Below, they are included in revitalized bone marrow, which lays down on their endosteal surfaces new bone, above they are still untouched by the process of organization and lie in necrotic bone marrow. This clearly shows that there was first the attempt at substitution of necrotic tissue by living tissue, which attempt was annihilated before it could fully reach its purpose.

Therefore, osteochondritis dissecans, as well as pseudo-osteochondritis dissecans, is not a clinical or pathologic entity. Both conditions are merely the morphologic manifestation of a secondary complication during the process of reorganization which primarily aims at complete substitution of a more or less extensive area of epiphysionecrosis. In one form of pseudo-osteochondritis dissecans it is the already reorganized and relatively small subchondral focus of necrosis which does not find osseous consolidation with the rest of the epiphysis, it remains separated by pseudoarthrotic fibrous tissue. In true osteochondritis dissecans a relatively much larger portion of the subchondral necrosis, not yet invaded by living fibrous tissue, is cut loose from the reorganized epiphysis by a more or less continuous zone of fibrous tissue. In both instances it is, without doubt, the use of the joint which interferes with the restitutio ad integrum of the epiphysis. Primarily, complete restitution can be expected in every case of reorganization of aseptic necrosis of bone. If adequate immobilization could be carried out at the critical period of the process, secondary trauma would not interfere with reorganization, and dissection would never occur.

Thus, trauma is certainly of great influence on the final outcome. It is hardly of etiologic importance, however. In most cases the condition is bilateral and for this reason alone is more suggestive of constitutional than of traumatic factors. Besides, the history of almost all cases fails to include severe trauma. Of great interest in this connection is the case reported by Støren of a family of ten children with osteochondritic joint lesions occurring in the father and four children. Støren's case shows so clearly the importance of a constitutional and hereditary background in the formation of osteochondritic bodies that all attempts to introduce trauma as an etiologic factor seem to be far fetched. Questions of compensation, which will arise in view of the fact that most of the patients are workmen in the prime of life, will have to be considered accordingly, as was done in case 4. As long as nothing is known about the cause of "idiopathic" aseptic necrosis as long as physicians have only vague ideas concerning the possible duration of a process of reorganization which is hypothecated from the roentgenologic changes, the patient may benefit from the physician's ignorance. In case of doubt and uncertainty, one may decide in the

patient's favor If, as in case 4, roentgenologic findings contradict causal connection between aseptic necrosis and industrial accident, the claim will have to be considered on the ground that the trauma has occurred in a pathologic skeleton and will have to be rejected in most instances

Also of great practical importance is the question of hypertrophic arthritis in connection with osteochondritis dissecans The head of the femur in cases 4 and 6 was enlarged at the time of operation, there were large marginal exostoses, and the synovial tissue was decidedly hypertrophied The autopsy in case 3, however, showed diminution rather than enlargement of the affected femoral heads The explanation of this difference is probably as follows In case 3 the disease was certainly of much longer duration, and accordingly a much greater portion of the head of the femur had been lost by absorption

Another important factor is the use of the joint Hypertrophic arthritis does not necessarily complicate the picture of aseptic necrosis The joint cartilage primarily does not participate in the pathologic process, it will however, become affected secondarily by the deformation of the bony epiphysis (Axhausen's osseous form of arthritis deformans) The deformation, as already pointed out, will be the greater the more the joint is used during the active phases of the organizing process Hypertrophic arthritis never develops in a joint which is kept at rest There is no doubt that the patients in cases 4 and 6, laborers, used their hips more than did the patient in case 3, although I had only a scant clinical history in this case There are two facts, therefore, to explain the relative smallness of the femoral heads in case 3 there was more bone absorption, because of the longer duration of the disease, and the hypertrophic arthritic changes were only mild because of the restriction of function The enlargement of the head, the mushroom deformity, can be considered as the result of overuse of a diseased joint

However, there is still another fact which is certainly of importance for the development of arthritic changes I mentioned in the report of case 6 the hole in the joint cartilage through which detritic material oozed into the free joint cavity with every increase in the intra-articular pressure A similar oozing must have taken place in case 4, in which there were multiple fractures of the joint cartilage with a spicule of bone protruding toward the joint cavity at the end of the subchondral fracture space I also mentioned the constant irritation of the synovial membrane by this seeping of necrotic powdered material into the joint The reactive hyperplastic changes of the synovial capsule and the active cartilaginous proliferation at the joint margins were certainly due in part at least to this articular irritation

It may be that such a perforation of the joint cartilage is a "safety valve" in cases of epiphysioneclerosis. If the pressure within the subchondral fracture and marrow spaces rises above a certain level by the accumulation of ground-up calcified material, the latter can escape through the hole of the joint cartilage into the joint cavity, thus decreasing the pressure within the bony epiphysis. Exactly the same mechanism was observed by Pich¹³ in her case of traumatic Perthes' disease.

Treatment for the patients belonging to the second group is not as simple as for those of the first group. Deformation of the femoral head is usually marked, osteochondritis dissecans being a late complication of reorganization of aseptic necrosis. Physical therapy may temporarily relieve symptoms, but it will not have lasting effect. For advanced and extensive epiphysioneclerosis one must consider surgical intervention. No one, however, who has ever seen such a femoral head will think with Moucher that the removal of the dissected portion is an easy or advisable procedure. As practically the entire joint surface is involved, removal of the necrotic area will deprive the head of the femur of its joint cartilage and will increase and not alleviate the deformity. Only radical procedures can be of help: either arthrodesis or arthroplasty. Arthrodesis is certainly the safer procedure, but it should be resorted to only if the condition is unilateral. I should never recommend arthrodesis for bilateral conditions. One hip is usually more affected and may be the only one that bothers the patient. If this hip should be fused, it is probable that within a short time after the operation the same symptoms which led to the fusion operation would develop in the other hip. I feel, therefore, that arthroplasty is the wiser procedure. I performed it in cases 4 and 6. The result in case 4 at the time of writing, two years after the operation, is gratifying to both the surgeon and the patient. In case 6 the operation was done too recently to permit one to judge the result. The arthroplasty in this case was combined with a wedging out of the greater trochanter according to Albee's technic in order to reconstruct the length of the neck and to overcome the insufficiency of the abductors.

13 Pich, G. Histopathologic Study in a Case of Perthes' Disease of Traumatic Origin, *Arch Surg* **33** 603 (Oct) 1936.

PARTIAL THORACOPLASTY WITHOUT DEFORMATION

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All surgical methods pass through three stages first, the pioneer stage, during which the surgeon is happy if the operation has been successful, that is to say, if the patient has survived it, then the second stage, in which, the rate of mortality having diminished, the surgeon endeavors to render the operation more efficacious, and finally the third stage, in which he tries to perform an efficacious operation with as little mutilation as possible

Surgical treatment of pulmonary tuberculosis has already passed the first two stages It no longer endangers life, and it is efficacious This is the result of thirty years of continued effort on the part of surgeons all over the world At present the problem consists in performing the operation without mutilating the patient

Examination of a patient on whom a routine thoracoplasty has been performed reveals that the deformity he presents is due to three causes (1) vertical lowering of the scapula with subsequent fall of the shoulder, (2) sinking in of the scapula into the depth, this bone being also projected laterally, and (3) scoliosis, with convexity toward the side on which operation was done Scoliosis when slight may not be noticed, but when accentuated it may cause considerable deformity

For a long time it was thought that this deformity might be due to the thoracic collapse, however, close observation of the static condition of the scapular girdle indicates that the latter, essentially leaning on the sternum through the clavicle and attached to the spine by means of the muscles of the scapula, forms a sort of vault under which the thorax is set It is therefore possible to collapse the apex of the thoracic cavity completely without involving the scapular girdle, provided the muscles are spared as much as possible

As a matter of fact, the displacement downward of the lower part of the shoulder blade is due to section of the trapezius, the levator scapulae and the rhomboid muscle, which normally suspend this bone The lateral displacement is due to section of the rhomboid muscles, which allows the scapula to slide outward The sinking of the scapula

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into the depth of the cavity produced by the thoracoplasty is due to the pull of the collapsed thoracic wall through serratus magnus, since this muscle unites the posterolateral portion of the thorax to the spinal border of the scapula. This sinking is not due to loss of the osseous support of the scapula, as it is still in contact at its angle with the seventh and eighth ribs. On the other hand, the pull of this muscle opposed by the scapula also prevents the collapse from being as complete as it might be. Therefore, whereas the muscles which hold the scapula should be respected by the surgeon, it is important to sever the serratus magnus.

As regards scoliosis, the pathogenesis of this complication has been extensively discussed. Hug¹ in Germany, Bisgard² in America and recently Cleveland³ all have studied the question thoroughly. It is evident that the greater the number of ribs resected, the greater the risk of scoliosis, this, however, is not an absolute rule, and according to our own experience thoracoplasty may be performed without the rectitude of the spine being affected if the integrity of the laterovertebral muscles is preserved, as this important mass can prevent an exaggerated deviation. Important deformities are observed (1) when these muscles have been slashed in an attempt to find the neck of the rib (this method is, we believe, now abandoned by all surgeons) and (2) when the portions of the skeleton into which these muscles are inserted, namely the transverse processes of the vertebrae, have been removed.

It is our opinion that from the orthopedic point of view the removal of the transverse processes of the vertebrae is a mistake. The efficacy of this procedure in treatment of tuberculous lesions is doubtful. Moreover, it has become unnecessary since the introduction of Semb's technic for extrafascial apicolysis, which makes it possible to free the lung from the skeleton. Extrafascial apicolysis is unquestionably an improvement in pulmonary surgery, because, as it includes both lateral and vertical collapses, fewer bones have to be sacrificed than in ordinary thoracoplasty, which produces only a transverse mobilization.

The time is past when surgeons proudly added up the length of the ribs they had resected, happy when the total exceeded 1 meter. At present the surgeon's ambition is to obtain the best possible collapse with the least possible costal resection.

1 Hug, O. Thorakoplastik und Skoliose, *Ztschr f orthop Chir* (supp) 42 1, 1921

2 Bisgard, J. D. Thoracogenic Scoliosis. The Influence of Thoracic Disease and Thoracic Operations on the Spine, *Arch Surg* 29 417 (Sept) 1934, Skeletal Deformities in Children Resulting from Empyema and Methods of Prevention, *J Thoracic Surg* 6 609 (Aug) 1937

3 Cleveland, M. Lateral Curvature of the Spine Following Thoracoplasty in Children, *J Thoracic Surg* 6 595 (Aug) 1937

One may conclude, therefore, that to cause no deformity thoracoplasty should not involve the trapezius muscle, the angular and rhomboid muscles or the latissimus dorsi muscle, since these muscles fix the scapula. In view of this, many authors have proposed a lateral axillary incision which cuts into only the serratus magnus. Such an incision, unfortunately, provides an insufficient opening precisely at the site where an opening is most needed, a simple thoracoplasty by this method is difficult, and Semb's operation could not even be considered.

Whence the interest of muscular dissociation, the possibility of which was demonstrated on the abdomen by McBurney.³ Picot⁴ of Lausanne, Switzerland, was the first surgeon who tried to operate on the thorax by dissociating the muscular fibers of the trapezius and rhom-

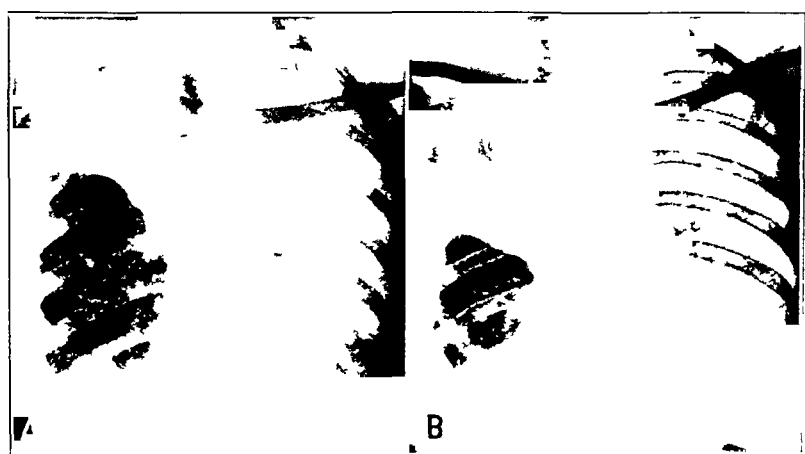


Fig 1 (case 1) —A, cavitation of apex, of two years duration. A one stage extrafascial apicolysis was performed, with resection of five ribs. B, result six months after operation. Cultures of the sputum were sterile, and the patient was apparently cured.

boideus muscles without cutting the fibers. Picot used a transverse or slightly oblique interscapulovertebral incision which enabled him to perform either an endofascial apicolysis or a small thoracoplasty.

By modifying the direction of Picot's incision and cutting some of the trapezius fibers (the ascending fibers which play no part in fixation of the shoulder) we were able to perform thoracoplasties involving as many as six ribs and to perform extrafascial apicolysis.

4 Picot in Bernou A, and Fruchaud H. *Chirurgie de la tuberculose pulmonaire. Indications techniques, résultats*. Paris: Gaston Doin & Cie, 1935.

5 Iselin, M. *L'apicolyse extra-fasciale (methode de Semb)*. *Presse med* 45:1539 (Nov 3) 1937. Iselin M and Dupan R. *Technique de l'apicolyse extra-fasciale totale*. *J de chir* 52:748 (Dec) 1938.

under conditions far more favorable than those obtained in making the usual incisions around the scapula

The cutaneous incision is oblique, starting at the seventh cervical vertebra (the prominent one) and extending as far as 3 cm below the angle of the scapula. The upper part of the incision does not have to reach the seventh cervical vertebra but starts at 1 cm from it, if necessary, its lower extremity may be prolonged along the spinal border of the scapula

Therefore, this incision coincides at its upper extremity with the posterior part of the first rib and at its lower extremity with the anterior part of the first rib. It allows a favorable approach to the most difficult point in surgical treatment of pulmonary tuberculosis ablation of the first rib, the key of the thoracoplasty

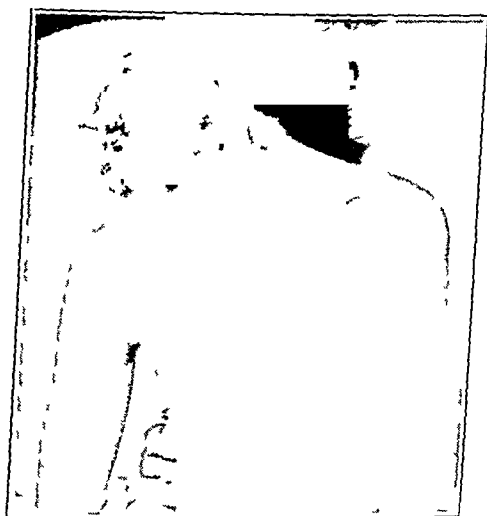


Fig 2 (case 1) —Patient one month after operation

The skin having been incised and freed on each side, the trapezius muscle is dissected between two of its transverse fibers, that is to say, at the level of the upper angle of the scapula. Then, almost perpendicularly, the ascending fibers are cut 1 cm from their attachment to the bone, the débridement is effected over 4 to 5 cm. Immediately underneath, one finds the rhomboid muscle, the oblique fibers of which are exactly parallel with the incision. One cuts between the muscular fasciae at the middle portion of the wound. Two retractors are placed, and when the scapula is retracted laterally a small portion of the costal grill, usually in the vicinity of the third and fourth ribs, comes into view.

Through a longitudinal incision along its external border, the latero-vertebral muscular mass is separated from the costal plan, and it is then easily retracted as far as the transverse processes of the vertebra by means of Semb's retractors.

The medial aspect of the rib is now exposed. To put the lateral aspect in evidence, the surgeon's assistant pulls on the scapula and stretches the serratus magnus muscle, which is cut so as to put the anterior extremity of the rib within reach. Alexander was wise in insisting on this maneuver.

However, the opening obtained is not considerable. The fourth rib should be carefully disarticulated and resected over 8 to 10 cm. The third rib is then much more easily viewed, it also is resected and disarticulated, the third rib can be resected much more easily than the fourth. Then the second rib appears and is entirely freed and resected. When the second rib has been removed, the first rib appears and, once the serratus magnus and the posterior scalene muscle have been cut, it is viewed from end to end on both superior and inferior aspects.

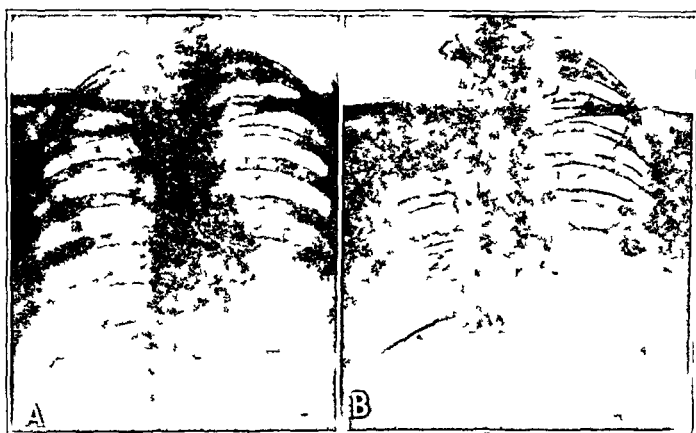


Fig 3 (case 2)—*A* extensive cavitation of the right apex of five years' duration. *B*, result six weeks after operation (a one stage extrafascial apicectomy, with resection of five ribs).

The surgeon who has never used this particular incision will be surprised to find that with its use the ribs can be viewed one after the other. However, this is anatomically logical since when seen from the posterior aspect the first three ribs appear not vertical but horizontal one before the other. Such an incision fits in with the surgical needs. The nearer one gets to the difficult and dangerous area, the better the view provided, whereas the usual incision around the scapula opens into a sort of well the bottom of which is deep and inaccessible. Extrafascial apicectomy is much more easily performed with the incision described, since the apex of the lung is exactly in the center of the wound.

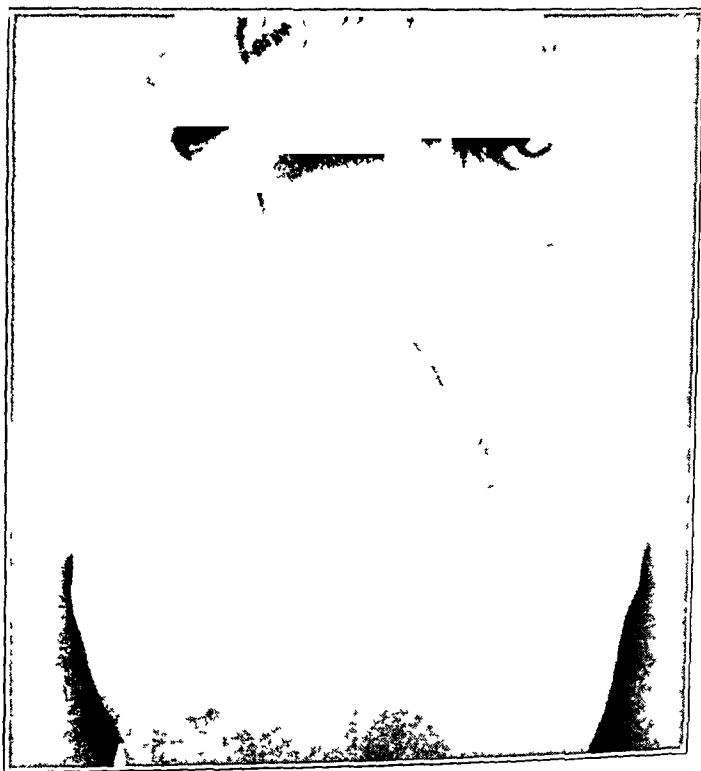


Fig 4 (case 2) —Patient six months later The sputum was sterile, and the patient was apparently cured



Fig 5 (case 3) —*A*, extensive cavitation into incomplete artificial pneumothorax *B*, roentgenogram taken on discharge of the patient, three weeks after the operation Six months later the sputum was sterile and the patient apparently cured

Of course, it is necessary to have at one's disposal a set of instruments suitable for the purpose since the mere introduction of the surgeon's hand into the incision obliterates the entire operative field. Everything has to be done with forceps, even the knots. The compresses must also be handled with forceps. Our equipment, manufactured by Collin, in Paris and partly inspired by Semb's equipment, is simple. It includes

- 1 Two Semb retractors for retracting the laterovertebral mass inward without injuring it

- 2 Two strong double-bent retractors the larger for retracting the scapula outward and the smaller for retracting the trapezius muscle upward. Naturally, one should never retract medially and laterally at

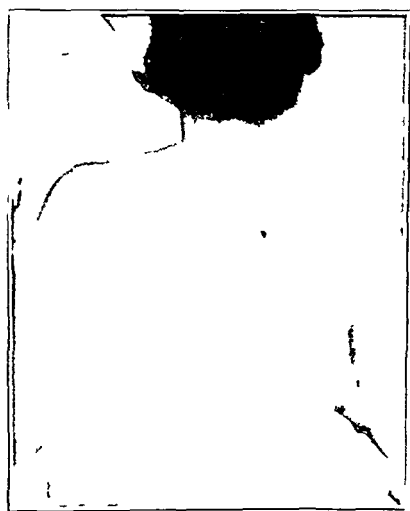


Fig. 6 (case 3)—Patient two weeks after operation (a one stage extracostal apicolysis, with resection of four ribs)

the same time, as the incision would be too small. For working on the outer and anterior regions the surgeon uses retractors with a handle. For working medially, the traction is best provided by Semb retractors.

- 3 Three rugines, one for the outer face, one for the border and one for the deep face of the rib. Each one cuts only at the precise site where cutting is needed, all the remainder of the instrument being blunt. This is the reason for the semicircular shape of the instrument.

- 4 Brunner's costostome for costostomy. We had the instrument made however with a double-bent stem so that the hand holding it would not hide the incision. Because of this double bending and because of its length it is possible to push this costostome very far inside and to watch its extremity and know exactly what is being cut.

It is needless to emphasize the advantages of this incision. It provokes little hemorrhage, and, as the muscle is not cut, it does not cause shock. A surgeon accustomed to this technic can easily resect six ribs if necessary. Reconstruction is extremely simple: the ascending fibers of the trapezius muscle which have been cut must be carefully sutured, in this region the trapezius adheres to the aponeurosis so that one has only to stitch in the latter. The dissociated muscular parts are brought together by means of two sutures, as in McBurney's incision.

The results are excellent. For the past two years we have resorted to this incision for all thoracoplasties and extrafascial apicolyses. The accompanying photographs and roentgenograms show the extraordinary morphologic preservation, in contrast with the considerable degree of thoracic collapse obtained.

APPENDICITIS

WITH SPECIAL REFERENCE TO PATHOGENESIS, PATHOLOGY AND TREATMENT

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OMAHA

INTRODUCTION

The thesis that appendicitis in the majority of cases is a form of closed loop obstruction will be developed in this paper. It will be shown that in 80 per cent of all cases in the series the condition was on an obstructive basis and that in 67 per cent an impacted fecalith was the obstructing mechanism. It will be demonstrated that there is a direct correlation between the presence of a fecalith and subsequent development of obstruction with closed loop formation, eventuating in perforation and peritonitis if the obstruction is not overcome by expulsion of the fecalith or release of the obstruction by other means.

As early as 1846 this sequence of events in appendicitis was noted by Volz¹ in his monograph. He reported 46 cases in which such a series of events was observed, and he mentioned five other authors who had seen a similar pathologic picture (fig 1). In 1847 Gerlach² reported a case in which the fecalith was said to have been as large as a hazelnut. In his epochal paper in 1886 Fitz,³ of Boston, made similar reference to the high incidence of fecaliths and obstruction, especially in cases of perforation. Pozzi,⁴ in 1897, emphasized the fact that in appendicitis the appendix behaves as does any other closed loop. In

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Abridgment of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Surgery

1 Volz, A. Die durch Kotsteine bedingte Durchbohrung des Wurmfortsatzes, die häufig verkannte Ursache einer gefährlichen Peritonitis und deren Behandlung mit Opium, Carlsruhe, C. F. Müller, 1846

2 Gerlach, A. Beobachtung einer tödlichen Peritonitis als Folge einer Perforation des Wurmfortsatzes, Ztschr. f. rat. Med. 6 12-23, 1847

3 Fitz, R. H. Perforating Inflammation of the Vermiform Appendix with Especial Reference to Its Early Diagnosis and Treatment, Am. J. M. Sc. 92 321-461, 1886

4 Pozzi, M. S. Pathogenie de l'appendicite, Presse med. 1 1-4, 1897

his monograph in 1908 Maalp⁵ cited Iverson, Reclus, Roux, Treves and Dieulafoy as saying that appendicitis usually is a sequel to obstruction of the lumen and formation of a closed cavity. Morison and Saint⁶ noted the danger of tension gangrene following obstruction of the lumen of a hollow viscus, such as the appendix.

There is much of interest in the history of appendicitis, but it has been well discussed by Deaver,⁷ Kelly and Hurdon,⁸ Royster,⁹ Collins¹⁰ and many others, so that no attempt will be made to cover that phase of the subject here.

THEORIES OF ETIOLOGY

There are seven main theories (Krecke¹¹) with regard to the etiology of appendicitis. A critical discussion of each follows.

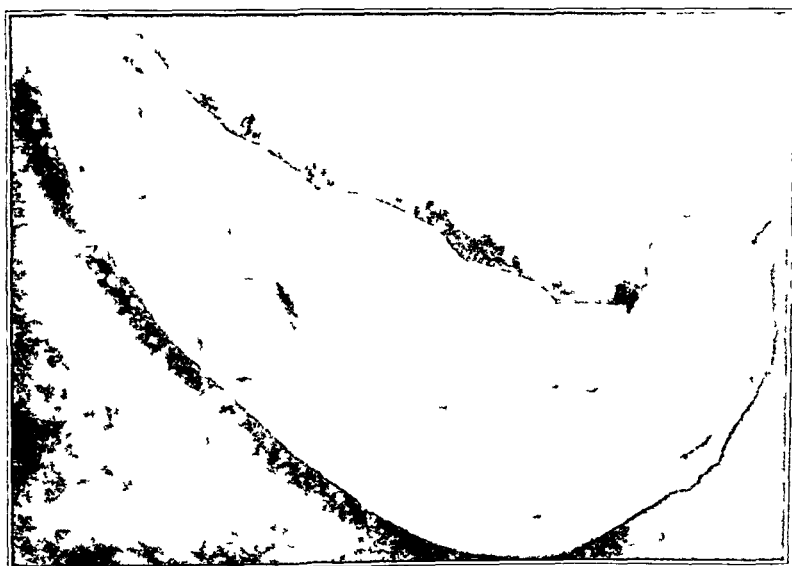


Fig 1—Longitudinally sectioned appendix, demonstrating the distention of the lumen and thinning of the walls seen in appendices obstructed by an impacted fecalith. This is the typical picture seen when the obstruction has existed long enough for tension gangrene to supervene.

5 Maalp, C. U. *Histopatologiske studier over processus vermiformis*. Copenhagen, 1908.

6 Morison, R. and Saint, C. F. M. *An Introduction to Surgery*, Baltimore, William Wood & Company, 1935.

7 Deaver, J. B. *Appendicitis*. Philadelphia: P. Blakiston's Son & Co., 1896.

8 Kelly, H. A., and Hurdon, E. *The Appendix and Its Diseases*, Philadelphia: J. B. Lippincott Company, 1911.

9 Royster, H. A. *Appendicitis*. New York: D. Appleton and Company, 1927.

10 Collins, D. C. *Historic Phases of Appendicitis*, *Ann Surg* **94**: 179-196, 1931.

11 Krecke, A. *Ueber die Ursachen und das Wesen der Appendizitis*. *München med Wchnschr* **80**: 299-302, 1933.

1. *Infectious Origin*—(a) *Enterogenous* In view of the fact that the dictums of Aschoff have been generally accepted for many years, they will be discussed first. Aschoff¹² stated that infected fecal matter comes to rest in one of the permanent rugations of the appendical mucosa and that owing to stasis the organisms, usually gram-positive diplococci, increase in virulence so that they are able to penetrate the mucosa. A wedge-shaped area of inflammation then develops, and while the main reaction in the distal third of the appendix is mucosal, the organisms spread rapidly up the lymph spaces of the submucosa, so that in the proximal third the serosa is most severely involved. Not simple retention of feces but stagnation of the special content of the appendix is responsible for appendicitis, according to Aschoff, and he stated definitely that in every case acute appendicitis develops on the basis of a local enterogenous infection in an especially susceptible, or "prepared," appendix. Fecaliths, he stated,¹³ act only by aiding stasis and retaining bacterial toxins. Aschoff was able to isolate pure strains of a gram-positive diplococcus from the distal third of the appendix, and he concluded that these unsociable organisms, which do not mix with the ordinary fecal flora, are the sole cause of appendicitis, being as specific as the gonococcus or the tubercle bacillus.

There are a number of serious objections to the views of Aschoff. First, no one has ever been able to confirm his statement that the appendix contains a special type of flora unmixed with fecal organisms. In Europe diplococci apparently form a prominent component of the human fecal flora, but in the United States they are comparatively uncommon, except in laboratory animals. Second, no one has ever been able to find the wedge-shaped area of primary infection, and Aschoff himself said that unfortunately he has not been able to demonstrate it on section. Furthermore, it never has been shown that stasis of organisms increases their virulence, rather, it has been proved that stasis weakens a strain because of the development of bacteriophage and degenerative forms. Moreover, it has been shown that the best way to increase the virulence of a bacterial strain is by rapid passage through a series of laboratory animals. It cannot be shown that the inflammation spreads proximally from the site of origin, as it should if Aschoff's theory is correct. In fact, in this series the inflammation was always distal to the point of obstruction and faded off to a normal condition near the base, unless the obstruction was at the base, in which

12 Aschoff, L. Pathogenesis und Aetologie des Appendicitis, *Ergebn d inn Med u Kinderh* 9 1-30, 1912, *Appendicitis Its Aetiology and Pathology*, translated by G C Pether, London, Constable & Co, Ltd, 1932.

13 Aschoff, L. Ueber die Bedeutung des Kotsteines in der Aetologie der Epityphilitis, *Med Klin* 24 587, 1905.

instance the entire organ was involved. If appendicitis is a bacterial disease bacteria should be present in the tissues at an early stage. Actually, it will be shown that in only 20 per cent of cases of acute appendicitis are bacteria present in the tissues, whereas the incidence increases to 60 per cent in the gangrenous specimens. Thus, if the organisms appear late in the course of the disease, or not at all, they cannot logically be assumed to play an important etiologic role. Bacterial toxins need not be invoked as a cause of inflammation, for it can be shown that appendical inflammation will develop in a sterile appendix as a result of osmotic imbalance (Bowers ¹⁴). It can be shown further ¹⁵ that in a closed loop of the appendix with complete retention of bacteria and toxins no inflammatory changes occur unless distention of the loop supervenes. According to Aschoff, gangrene develops on the basis of vascular thrombosis, but if this were true there would be no distention of the lumen with thinning of the walls. In all cases of obstruction in this series the lumen was dilated and the wall was thinned,

TABLE 1—*Observations in a Case of Obstructive Appendicitis**

Region	Gross Changes	Fecalith	Wall	Lumen	Reaction in Sections	Results of Gram Stain
Tip	Gangrene		Thin	Distended	Extreme	Bacteria in mucosa
Midzone	Gangrene	Impacted	Thin	Occluded	Some	Negative
Base	Acute		Normal	Normal	Slight	Negative

* The inflammation is severe, distal to the point of obstruction. Proximally the lumen is normal and the walls of the appendix show slight reaction. This would not be true if the dictums of Aschoff were correct.

owing to distention. There were few instances of gangrene without obstruction, but in these cases there was no distention or thinning. The walls were thick and soggy owing to accumulation of inflammatory exudate. In the animal series, ¹⁵ gangrene of the cecal appendage due to vascular damage was not accompanied by thinning or distention.

The objections to Aschoff's views are demonstrated in the data relative to a typical clinical case (table 1). According to the other theory of the enterogenous infectious origin of appendicitis, swallowed organisms from foci in the nose and throat set up an inflammatory process in the appendix. In support of this view, similar organisms are said to have been isolated from the throat and from the appendix, but this does not prove their pathogenicity nor is it remarkable that organisms which are constantly being swallowed might be cultured from

14 Bowers, W. F. Role of Distention in the Genesis of Acute Inflammation of Hollow Viscera, *Am J M Sc* **194** 205-214 1937.

15 Wangenstein, O. H., and Bowers, W. F. Significance of the Obstructive Factor in the Genesis of Acute Appendicitis: An Experimental Study, *Arch Surg* **34** 496-526 (March) 1937.

any part of the intestinal tract. It also has been argued that the prevalence of dental caries and sinusitis explains the high incidence of appendicitis, but this is as fallacious as the idea that the condition is due to a tonsillar focus.

(c) *Hematogenous*.—According to this theory, the appendix serves as an abdominal tonsil and filters organisms out of the blood stream. These organisms are assumed to enter the blood stream from the region of the tonsil. It has even been stated that bacteria in the blood stream electively localize in certain organs. This, it seems, carries the idea of the bacterial origin of disease a bit too far. These points will be elaborated under subsequent captions. Suffice it to say here that no investigator has yet been able to isolate organisms from the blood stream in cases of appendicitis with any degree of frequency. Many series of cases have been reported, but the incidence of blood cultures yielding bacteria is negligible. In 1 case in this series a blood culture contained *Bacillus coli*. The patient had otitis media and mastoiditis with sinus thrombosis caused by this organism, but the bacteremia was secondary to perforation and generalized peritonitis. The patient died one month after appendectomy.

2 *Neuroangiospastic Origin*.—Ricker concluded that gangrene occurs in appendicitis much earlier than can be accounted for on an infectious basis, and he therefore postulated the theory of vasospasm. He stated that appendicitis is comparable to Raynaud's disease and that gangrene develops because of ischemia of the appendix. This theory has been violently attacked by Aschoff, and, indeed, the finding of a pale, bloodless, gangrenous appendix at operation must be a rare occurrence. The usual appearance is one of turgescence and venous congestion with actual hemorrhage into the tissues. The theory of Ricker is not borne out by observation of clinical cases.

3 *Endemic Origin*.—Familial and institutional outbreaks of appendicitis have been reported, and the question of contagion also has been raised. These "epidemics" are more apparent than real, however, and it will be shown subsequently that the incidence of appendicitis is fairly constant, there being no seasonal variation if observations are carried on over a long period. It is thought that endemic and familial outbreaks are best accounted for on the basis of similar faulty diet or familial poor anatomic arrangement of the appendix, as will be mentioned later.

4 *Dietary Origin*.—The fact that there are so few cases of appendicitis among some peoples, such as the Arabs, the aboriginal Negroes, the Turks, the Persians and the Dutch, has led to the theory that appendicitis is a result of modern diet. It has been reported that

there were but 2 persons with appendicitis among 86,000 clinic patients seen in Tientsin China. Bearing out the idea of the importance of diet is the fact that in the small series of cases reported here gangrenous appendices occurred in 2 Chinese students. One of the appendices was obstructed by a fecolith. Pales¹⁶ found a low incidence of appendicitis among South African natives, associated with a high incidence of a funnel-shaped appendicocolic junction. There may be a similar anatomic explanation for the low incidence of appendicitis in other races. Murray¹⁷ quoted Williams as saying that as a result of beef and mutton fats in the diet calcium soaps are formed in the walls of the appendix. It has been asserted that these insoluble soaps may form a complete ring and produce various complications. It is difficult to see, however, why this deposit should be limited to the appendix. How much more serious such a ring of soap would be in the small intestine! Murray attempted to show that appendicitis develops in wild animals maintained in captivity and cited the low incidence of the disease in the so-called primitive races. Short¹⁸ also mentioned the effect of civilization in causing appendicitis in captive higher apes. The flaw in this theory is that one has no means of knowing what are the usual causes of death among apes in their native jungles. The increased use of iron rollers in grinding grain for flour has been suggested as a cause of appendicitis. It is said to lead to a decrease in cellulose in the diet, with consequent development of constipation, increase in virulence of organisms and appendicitis. As will be shown later, however, rather large amounts of cellulose and vegetable fibers actually are found in the obstructing fecaliths. It seems from this that a decrease in intake of cellulose might reduce the number of fecaliths, the cellulose often acting as a nidus about which the fecalith forms. Appendicitis has been attributed to the increased use of food preservatives and the higher percentage of meat ingested. Some significance may be attached to this statement, as it has been shown by Wilkie¹⁹ that closed loops containing protein material rupture much earlier than others because of rapid putrefaction and formation of gas. Egdahl²⁰ has shown that the incidence of appendicitis in the Filipino and Puerto Rican units of the United States Army is correlated with

16 Pales, L. Appendice et appendicite chez le noir en Afrique equatorial française, *Ann d'anat path* **11** 563-583 1934

17 Murray, R. W. Geographical Distribution of Appendicitis, *Lancet* **2** 227-230, 1914

18 Short, A. R. Causation of Appendicitis *Brit J Surg* **8** 171-188 1920

19 Wilkie, D. P. D. Acute Appendicitis and Acute Appendicular Obstruction, *Brit M J* **2** 959-962 1914

20 Egdahl, A. Some Etiological Factors in Acute Appendicitis *Mil Surgeon* **73** 61-69, 1933

the incidence of beriberi. He has shown also that the incidence of appendicitis is low when these troops are fed on their native diet but increases markedly when they are given the same diet as white troops. Here again, the factor of constipation and fecalith formation may be important. Egdahl also stated that in student health services there is a significant grouping of cases after the Thanksgiving and Christmas holidays, on a basis of dietary indiscretions. It is well known among pediatricians that children frequently have attacks of acute appendicitis after a particularly heavy meal. This tendency is based on the fact that the increased secretory and peristaltic activity may initiate a pressure-distention mechanism in the appendix. The use of water closets instead of the squatting position in defecation has been said to increase the incidence of appendicitis, on the assumption that the new position favors constipation. Mercier, in scorn at these peculiar suggestions, suggested the abandonment of wig wearing as the cause of appendicitis.

5 *Traumatic Origin*—Shutkin and Wetzler²¹ concluded that traumatic appendicitis may occur in some cases, and there seems to be a logical explanation for its pathogenesis. The appendix may be crushed against the ilium or the spine, with resulting infarction or gangrene. Wangenstein and Bowers¹⁵ have shown experimentally that vigorous pinching of the appendix is followed by inflammatory changes. This type of gangrene is not accompanied by distention or thinning of the walls of the appendix. The appendix may be overdistended suddenly by a blow on the abdominal wall so that it is actually ruptured, or it may be so severely stretched that rents in the mucosa occur and infection develops. If the appendix happens to contain a fecalith, trauma may impact the fecalith or edema may so reduce the diameter of the lumen that a small fecalith will occlude it. In either event a closed loop is formed, with all of its potentialities. There is no doubt that trauma may cause appendicitis in some cases. In this series, 1 patient gave a history of having been kicked in the abdomen on the day previous to the attack. The appendix was gangrenous and was obstructed by a fecalith. The significance of the trauma cannot be evaluated.

6 *Foreign Body Origin*—Monographs on appendicitis have listed lead shot, pins, bristles, various types of seeds, spicules of bone, enamel from cooking vessels and many other types of foreign bodies as having been seen in the appendix in addition to fecaliths. One theory is that a foreign body, by its mere presence in the lumen, sets

²¹ Shutkin, M. W., and Wetzler, S. H. Traumatic Appendicitis, *Am J Surg* 31: 514-520, 1936

up an acute inflammatory reaction and erodes through the wall. That this is not necessarily true is shown by the fact that foreign bodies often are seen in the appendix during routine autopsies. The deciding factor in the development of inflammation is whether the foreign body occludes the lumen, forming a closed loop. Foreign bodies may cause appendicitis in one of two ways. They may actually erode or pierce the wall introducing infection, or they may occlude the lumen and form a closed loop. Formerly it was thought that a foreign body acted by causing stagnation and allowing increase in virulence of the retained organisms. It is now known that the consequent distention of the closed loop rather than retention of bacteria or their products causes appendicitis.

7 Mechanical Origin—That mechanical factors may be of great importance in the causation of appendicitis is not a recent idea. It was advocated in 1897 by Pozzi,^{*} who accredited the original concept to Dieulafoy. Pozzi stressed the mechanical effect of the valve of Gerlach in converting the appendix into a closed loop. Many experiments have been performed in which various foreign bodies were placed in the appendix, but the dictums of Aschoff have been so generally accepted that whenever acute inflammatory changes resulted it was said that the mechanical factors had caused retention of bacteria with consequent increase in virulence. These experimental results will be discussed under another caption, and the probable course of events in the genesis of appendicitis from the mechanical standpoint will be elaborated later.

Summary—There are only two distinct theories of the causation of appendicitis, the others being related merely to contributing factors. Infection and obstruction are the two etiologic agents, the latter operating in the majority of cases. Trauma may set either mechanism in motion, while diet and foreign bodies may be the initial cause of obstruction. As will be shown later, bacteria enter the picture even in cases in which the condition is due to obstruction, for they may cause increased damage to the tissues after primary vascular occlusion from obstruction. If it were not for the presence of bacteria, rupture of a closed loop of appendix would be harmless, therefore although obstruction is the cause of appendicitis in most cases bacteria are responsible for most of the fatalities.

STATEMENT OF THE PROBLEM

1 Approach—Wangensteen and I¹⁵ have shown in a large experimental series that obstruction and infection are the two most important factors in producing inflammatory changes in the cecal appendage of the dog. We showed further that increase in intraluminal pressure

is the most important factor in the genesis of acute inflammation. Intraluminal pressures of 6 and 15 cm. of water maintained for six to eighteen hour periods caused acute inflammation which progressed to gangrene in the longer experiments. I have shown¹¹ that acute inflammation develops in hollow viscera owing to obstruction and to hydraulic or osmotic imbalance even in the complete absence of the factor of infection. Maintained distention of the sterile renal pelvis or of the eye, for example, has produced all the changes associated with acute inflammation.

2 Purpose of This Study—These and other observations make pertinent this investigation, in which an attempt is made to determine whether the obstructive factor is present in clinical appendicitis and in what proportion of cases such a mechanism operates. It also is proposed to explain the pathogenesis of appendicitis and to evaluate the importance of bacteria in this process. Fecaliths are studied from the standpoint of their origin and their chemical composition. Other etiologic and pathologic factors in appendicitis are investigated from analysis of clinical cases.

MATERIAL AND METHOD

The material consisted of all the appendices removed at the Minneapolis General Hospital during 1935, together with a selected group of autopsy specimens, and all the appendices removed at the University Hospitals in 1936. This material included a selected group of appendices removed incidentally during some other surgical or gynecologic procedure. There were 485 specimens in the entire series, and they were divided into appropriate groups, depending on the pathologic picture.

All the specimens were fixed in a 10 per cent concentration of solution of formaldehyde U. S. P., in a large, flat dish, and after twenty-four hours were "bivalved" longitudinally in order to study the incidence of obstruction of the lumen due to fecaliths, strictures, kinks and other mechanical agencies. The specimens then were sectioned longitudinally, and these sections, through the entire length of the organ, were stained with hematoxylin and eosin and by the Gram-Weigert method for bacteria in the tissues. In one group sections also were stained by the azocarmine technic in order to study the process of fibrosis in healing. An attempt was made to correlate the details of the history, physical findings and laboratory data with the pathologic picture in each instance. The clinical series were analyzed statistically. Various special procedures were employed in some groups, and these will be described under subsequent captions.

ANATOMY

1 Appendical Musculature—The surgeon usually thinks of the appendix as a narrow, blind pouch which readily may become converted into a closed loop by a variety of factors, such as appendicoliths, inspissated contents of the lumen, organic strictures, embryonic kinks, neuromuscular disturbances or abnormality of the basal valve of Gerlach.

That there are anatomic factors which predispose to the development of a closed loop has been shown by Westphal,²² who demonstrated that the appendicular musculature is normally heaviest and most active at the base. He showed on roentgen examination that peristalsis usually begins at the base and most often progresses toward the tip instead of attempting to empty the organ. He also showed that the lumen is bulbous which makes difficult the egress of material which has found its way into the lumen. This point is important in understanding why fecaliths which have been in the appendix for years suddenly become impacted near the base, owing to some strong peristaltic stimulus or to their slow increase in size by accretion. Wood²³ on the other hand stated that distal dilatation of the lumen is a characteristic roentgenographic finding in the pathologic appendix.

2 Appendicocecal Junction—It is known that of the several types of appendicocecal junction described by Treves²⁴ the infantile, or funnel form is least likely to allow obstruction at the base. The significance of this fact has been demonstrated by Pales¹⁶ who showed that the incidence of acute appendicitis among African natives is 0.03 per cent and who observed in a large series of autopsies that the conical type of implantation of the appendix into the cecum predominates. Treves described four anatomic types of appendical origin from the cecum: 1. In the fetal type the appendix arises from the lowest point of the cecal apex in a funnel-shaped manner. Sprengel²⁵ observed this type of origin in 25 per cent of cases, but Monrad,²⁶ in examining appendices of children, found it only in patients under 3 years of age. 2. In the transitional type the appendix springs from the cecal apex but is without the funnel-shaped base. 3. In another type the appendix arises just medial to the cecal apex. 4. In the fourth type the appendix arises from the most medial portion of the cecal apex, posterior to the ileocecal valve. Wangenstein, Buirge, Dennis and Ritchie²⁷ classified 262 appendices according to Treves' types and observed type 1 in 40 per cent, type 2 in 2 per cent, type 3 in 52 per cent and type 4 in 6 per cent. When the specimens were divided according to the age of the patient, they found that 67 per cent of the appendices of patients up to 11 years of age were of type 1. They studied 477 appendices with

22 Westphal, K. Appendicitis und Kotstein als Folge gestörter Appendixfunktion. *Deutsche med. Wchnschr.* **60**: 499-504 and 600-604, 1934.

23 Wood, F. G. Radiology of the Appendix. *Brit. M. J.* **1**: 640-642, 1935.

24 Treves, F. Lectures on the Anatomy of the Intestinal Canal and Peritoneum in Man. *Brit. M. J.* **1**: 415, 470, 527 and 580, 1885.

25 Sprengel, F. Appendicitis in Billroth, T. and Luecke, G. *Deutsche Chirurgie*, Stuttgart, Ferdinand Enke, 1906, no. 117.

26 Monrad, cited by Maalö.

27 Wangenstein, O. H., Buirge, R. E., Dennis, C., and Ritchie, W. P. Studies in the Etiology of Acute Appendicitis. *Ann. Surg.* **106**: 910-942, 1937.

reference to the diameter of the cecal orifice and found that 0.4 per cent of the orifices were more than 15 mm. in diameter, 17 per cent varied between 10 and 15 mm., 2 per cent between 6 and 10 mm., 32 per cent between 4 and 6 mm., 1 per cent between 2 and 4 mm. and 44 per cent between 0.5 and 2 mm., 2 per cent were 0.5 mm. in diameter. The cecal orifice was round in 23 per cent, oval in 32 per cent, irregular in 3 per cent, crescentic in 27 per cent and slitlike in 13 per cent.

3 *Appendicular Lymphoid Tissue*—The role of lymphoid tissue as a defense against acute appendicitis has been greatly overemphasized. Berry²⁸ has shown that the fetal appendix contains no lymphoid follicles. According to him, lymphoid tissue appears in fourteen days, functional lymph nodes are present in six weeks and the number of follicles increases until the age of 20 years, when decrease begins. By the age of 60 there are only traces of lymphoid tissue. This cycle of development and atrophy closely approximates the curve for the age incidence of appendicitis, so that at the time when there is the greatest amount of lymphoid tissue the incidence of appendicitis is at its peak. My observations on appendicular lymphoid tissue in patients ranging from premature infants to octogenarians parallel those of Berry.

4 *Mucosal Fold of Gerlach*—In 1847, Gerlach² described a mucosal fold at the appendicocolic junction, which he observed to be present in 3 of 9 cases. He stated that this valve promotes stagnation of contents and the formation of fecaliths. Treves stated that the fold or some modification of it is usually present. The presence of this fold has long been denied by anatomists, but Wangenstein, Burge and others,²⁷ in studies of the microscopic anatomy of the appendix, observed this fold to be definite in most instances. Of 526 specimens they observed the mucosal fold in 81.5 per cent. This fold completely obscured the cecal orifice of the appendix in 11 per cent, partially concealed it in 15 per cent and failed to cover it at all in 74 per cent. That the mucosal fold cannot function as a sphincter was shown by the fact that in specimens from adult patients it never contained muscle tissue.

ETIOLOGIC FACTORS

1 *Incidence of Appendicitis*—The 485 cases in this series have been divided into the following groups for study and classification:

	Acute Appendi- citis	Gangrene	Perfo- rative Appendi- citis	Appendec- tomy After Interval	Appen- dical Colic	Para- sites	Gyneco- logic Group	Autopsy Material
Minneapolis General Hospital	49	20	34	16	5	5	29	23
University Hospitals	43	57	4	131	0	8	33	0
Total	92	77	38	147	5	13	62	23

28 Berry, R. J. A. Vermiform Appendix of Man. Structural Changes Therein Coincident with Age, *J. Anat. & Physiol.* 40: 246-256, 1905.

The group of cases of colic includes those in which there were clinical signs of acute appendicitis and the specimens showed evidence of obstruction but microscopic sections showed no inflammation. The gynecologic group includes all specimens removed incidentally during a pelvic surgical procedure.

The difference in the number of cases of perforation of the appendix in the two series is explained by the difference in policy at the two institutions. At the Minneapolis General Hospital all patients with appendicitis are operated on immediately, even in the presence of generalized peritonitis, unless there are signs of a localizing abscess with regression of symptoms. At the University Hospitals, on the other hand, in any case of appendicitis in which perforation and peritonitis are diagnosed a conservative regimen is followed. This consists of duodenal siphonage through an inlying nasal catheter, abdominal hot packs and peroral administration of fluids. Appendectomy is performed six to eight weeks later, cases of this kind, therefore, fall into the "interval" classification. In the student health service at the University, patients with perforated appendices are operated on, and this accounts for the cases of perforation in the University series.

2 Age Incidence—The average age of the patients with acute appendicitis in this series was 22 years. The average age, expressed in years, for the various groups was as follows:

	Acute Appendicitis	Gangrene	Perforative Appendicitis	Appendectomy After Interval
Minneapolis General Hospital	20	26	27	19
University Hospitals	20	23	17	20

The difference in age in the cases of perforation of the appendix at the two institutions is explained by the fact that at the University Hospitals patients in whose cases perforation is suspected are operated on only in the student health service. This gives a lower average age than the series from a municipal hospital.

TABLE 2—*Spread of the Age Incidence, Expressed in Years*

	University Hospitals Series	General Hospital Series
Acute appendicitis		
Age of youngest patient	2	5
Age of oldest patient	69	56
Gangrene		
Age of youngest patient	5	8
Age of oldest patient	55	53
Perforative appendicitis*		
Age of youngest patient	15	6
Age of oldest patient	70	53
Interval appendectomy		
Age of youngest patient	4	11
Age of oldest patient	62	72

* The short spread of the age incidence in the group of patients with perforative appendicitis at the University Hospitals is due to the fact that these patients were in the student health service; no patient with perforative appendicitis being operated on in the general surgical service.

In computing the data for the obstructive and those for the nonobstructive types, it was found that at the Minneapolis General Hospital the average age was identical for the two types, while at the University Hospitals the patients with obstructive appendicitis were 6 years older on an average than those with the nonobstructive type. The patients in the entire series were distributed according to age groups, as follows:

	0 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	71 to 80	81 Up
Minneapolis General Hospital	8	42	24	5	1	7	3	0	2
University Hospitals	4	7	20	10	1	5	1	0	0
Average	—	—	—	—	—	—	—	—	—

Similar charts of the age distribution were made for the cases of obstructive appendicitis in the two series. These were found to correspond exactly to the age distribution for the entire series. The youngest patients in whom obstruction by a fecalith was found were a boy aged 3 years in the University series and a girl aged 5 years in the Minneapolis General Hospital series.

It seems to be well recognized that appendicitis is chiefly a disease of childhood and early adult life. The average age mentioned by Tasche and Spano²⁹ was 22 years, that given by MacCarty³⁰ was 23 years, and that given by Burgess³¹ was 26 years. These figures are comparable with the average age of 22 years in this series.

3 *Sex Incidence*—Tasche and Spano²⁹ reported that 61 per cent of the patients with acute appendicitis in the University Hospitals series were males. There were 67 per cent of males in this series. The incidence for males among the groups was as follows:

	Acute Appendicitis Cases	Gangrene Cases	Perforative Appendicitis Cases	Appendectomy Para After Interval Cases	Para sites
Minneapolis General Hospital	29 (59%)	11 (57%)	25 (73%)	11 (71%)	0
University Hospitals	17 (41%)	41 (73%)	4 (100%)	47 (86%)	0
Average	50%	61%	86%	53%	0

In the group of patients with the obstructive type 58 per cent were males, and in the group with the nonobstructive type, 56 per cent were males. No satisfactory explanation for this preponderance of males ever has been advanced, nor does the phenomenon of obstruction offer any explanation.

4 *Seasonal Variation*—Stone,³² Tasche and Spano²⁹ and most other authors have stated that there is a higher incidence of appendicitis

29 Tasche, L. W., and Spano, J. P. Analysis of Seven Hundred Consecutive Appendectomies, *Ann Surg* **94** 899-909, 1931.

30 MacCarty, cited by Tasche and Spano²⁹.

31 Burgess, A. H. A Clinical Lecture on an Analysis of Five Hundred Consecutive Operations for Acute Appendicitis, *Brit M J* **1** 415-418, 1912.

32 Stone, C. S., Jr. Acute Appendicitis in Children, *Arch Surg* **30** 346-356 (Feb.) 1935.

in the summer. In explanation of this statement it usually is said that there is a higher incidence of infections of the upper respiratory tract and gastrointestinal upsets at this time of year. If appendicitis is an obstructive phenomenon, there is no apparent reason why there should be a seasonal variation. This matter has been subjected to the following investigation. In a study of the incidence of acute appendicitis at the Minneapolis General Hospital (a large municipal charity hospital) over an eight year period, 1928 through 1935, it was found that the curve for the monthly distribution was practically a straight line, the greatest variation between any two months for this period being 25 cases. This does not favor a bacterial origin of appendicitis, but is in accord with the theory of an obstructive origin.

5 *Familial Tendencies and Epidemiology*—In this series no familial relation has been noted. However, from time to time the idea that appendicitis is a contagious disease has appeared in the literature. Fomio³³ stated that he observed 6 cases of the disease in one family and naively added that the total really was 8 if one wished to count a niece and a nephew. He mentioned another family in which there were 6 cases in five years, this would give the disease a rather long incubation period. Fomio and Rieder³⁴ went further and stated that in 49 per cent of a series of 667 cases they were able to establish a history of contact with patients having appendicitis. The fact that no hospital has ever found it necessary to isolate patients with appendicitis casts grave doubt on the infectious nature of the disease, and the interval between the occurrence of the condition in the same family is much too long to be explained on the basis of contagion. There is no doubt that some families show a greater incidence than others, but this does not prove the theory of infectious origin. The most logical explanation is that there is a similar poor anatomic arrangement in the members of a family or that the family diet is one which favors constipation and formation of fecaliths.

6 *Association with Acute Exanthems*—In this series a patient with measles was operated on for appendicitis as an emergency procedure but the appendix was grossly normal, on section the lumen was entirely obliterated, the tissue was sterile and there were no signs of acute inflammation. In another case a patient had measles three days after an appendectomy. The specimen in this case showed no acute changes but there was some fibrosis with lymphocytic infiltration indicating previous attacks. In 3 cases scarlet fever developed within the first

33 Fomio, A. Die Blinddarmenzündung, ihre infectiöse Ursache und ihr endemisches Vorkommen. Schweiz med Wchnschr 53 947-954 1923

34 Fomio, A., and Rieder. Zur Frage der Kontagionsmöglichkeit des Appendicitis, Schweiz med Wchnschr 58 597-608 1928

few postoperative days. The specimens were acutely inflamed or gangrenous but showed no changes which distinguished them from those usually seen in cases of severe appendicitis. One patient had scarlet fever twenty-four hours after appendectomy. The appendix was acutely inflamed, the lumen was distended, and the walls were thinned as in the cases of obstruction, but no definite mechanism of obstruction could be demonstrated. Another patient had scarlet fever seven days after appendectomy. The appendix was gangrenous, and the lumen was obstructed by a fecalith. In the other patient scarlet fever developed eight days after removal of a perforated appendix. The specimen showed evidences of intraluminal pressure and distention, but no definite mechanism of obstruction could be demonstrated. One specimen was obtained post mortem from a girl who had died of scarlet fever. The appendix was normal on microscopic section except for masses of blood pigment deposited around the lymphoid follicles. These masses probably represented the residual signs of hemorrhage into the lymph follicles. Obstruction to the lumen apparently had not taken place, and the tissues did not show the presence of bacteria. In the entire series reported here, the incidence of colds or sore throats immediately preceding the onset of acute appendicitis was only 4.5 per cent.

The literature is full of references to the association of acute appendicitis with acute tonsillitis, infections of the upper respiratory tract, scarlet fever, measles and mumps, but the exact relation is not yet clear. Many of the older writers, including Adrian,³⁵ have simply stated that such a relation exists. Anderson,³⁶ Equen³⁷ and many others have cited outbreaks of appendicitis accompanying epidemics of tonsillitis or so-called "intestinal flu." An analogy between the tonsil and the appendix usually is inferred by these authors. It now is fairly well recognized by most pediatricians that the abdominal symptoms accompanying infections of the upper respiratory tract are on the basis of mesenteric lymphadenitis (Goldberg and Nathanson³⁸) rather than of appendicitis. The lymphoid tissue of the appendix may, however, enter into the general reaction of lymphoid tissue to infection and may even bring about appendiceal obstruction due to the swelling of the

35 Adrian, C. Die Appendicitis als Folge einer Allgemeinerkrankung klinisches und experimentelles, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 7: 407-445, 1901.

36 Anderson, H. B. Appendicitis as a Sequel of Tonsillitis, *Am. J. M. Sc.* 150: 541-548, 1915.

37 Equen, M. Appendicitis Following Tonsillectomy. A Clinical Study, *Tr. Sect. Laryng., Otol. & Rhin., A. M. A.*, 1932, pp. 130-137.

38 Goldberg, S. L., and Nathanson, I. T. Acute Mesenteric Lymphadenitis. *Am. J. Surg.* 25: 35-40, 1934.

follicles This is the probable cause of appendicitis in the cases of this series in which the condition preceded clinical scarlet fever Pribam³⁹ postulated a lymphangitic form of appendicitis and stated that swallowed organisms from the tonsils cause diffuse cecitis, ileitis, appendicitis and mesenteric adenitis He concluded that the organism is a streptococcus Tonsillectomy is said to cure the condition by removing the focus

It frequently is stated that the acute exanthems predispose to acute appendicitis According to Hudson and Krakower,⁴⁰ there have been reported 40 cases of appendicitis occurring during an attack of measles, and according to Donnelly and Oldham⁴¹ in 5 cases appendicitis accompanied mumps Tasche and Spano³⁹ reported a 6 per cent incidence of infection of the upper respiratory tract preceding an attack of acute appendicitis, but this is somewhat higher than the incidence of 4.5 per cent reported here

7 *Relation to Weather*—Hagertorn⁴² worked out an ingenious idea He reasoned that since drying inhibits bacterial growth and humidity favors it, wet weather should be accompanied by a higher incidence of infections He then argued that in wet weather the tonsillar organisms should become more virulent and when swallowed ought readily to set up an acute appendical infection He plotted case records against barometric readings and atmospheric temperature, but unfortunately his theory was not borne out

8 *Incidence of Parasites*—In this series there was an incidence of pinworms in 3 per cent of cases, and the average age of the patients was 17 years In 100 per cent of cases these parasites were found in females Pinworms often were the central nidus about which a fecalith had formed, but there were always other parasites free in the lumen In no case could the parasites be seen to penetrate the appendical wall but artefacts in lymphoid follicles often gave the appearance of parasitic invasion Clinically, the condition in these cases was diagnosed from the history, physical examination and laboratory findings as acute appendicitis of mild type, but on section the appendices were normal or merely showed evidence of previous attacks There were obliteration

39 Pribam, B. O. Nabelkolik, lymphangitische Form der Appendizitis und Lymphangitis mesenterialis, München med Wchnschr 82 942-944, 1935

40 Hudson, H. W., and Krakower, C. Acute Appendicitis and Measles, New England J. Med. 215 59-64, 1936

41 Donnelly, J., and Oldham, J. B. Mumps and Appendicitis, Brit. M. J. 1 98-99, 1933

42 Hagertorn, A. Einige Bemerkungen zur Aetiologie der Appendizitis besonders ihrer Wellerungsabhängigkeit München med Wchnschr 80 613-614 1933

of the tip in 20 per cent of cases, evidence of obstruction in 100 per cent and bacteria in the tissues in 40 per cent. The last observation probably is correlated with the fact that there was distention of the lumen in every case.

The pinworm is the parasite most frequently seen in the appendix. Warwick⁴ presented the following data from a series of 2,344 appendices. The total incidence of pinworms was 2 per cent, and there were no characteristically distinguishing symptoms. The average age of the patients was 18 years, and the parasites were found in females in 93 per cent of the cases. There was no evidence that the parasites had penetrated the tissues except as a postmortem phenomenon.

9 Previous Attacks—It is significant to note that as the severity of the disease process increases the history of previous attacks becomes less frequent, because the seriously ill patients are subjected to appendectomy, whereas in patients with mild appendicitis the process may spontaneously subside many times before a physician is consulted. In this series there was a history of previous attacks in 38 per cent of cases, exclusive of the group in which appendectomy was performed after an interval. The history of previous attacks among the various groups was as follows:

	Acute Appendicitis		Gangrene		Perforative Appendicitis		Appendectomy After Interval		Appendical Cœle	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Minneapolis General Hospital	25	51	7	38	10	30	13	81	3	60
University Hospitals	22	71	25	45	1	25	131	100		60
Average		51		41		27		90		

There was a history of previous attacks in 36 per cent of the cases of obstruction as compared with 57 per cent of the cases in which obstruction was not present. This also is a significant observation, indicating that in appendicitis due to obstruction there is less tendency to spontaneous recovery without operation.

In Stone's³² series there was a history of previous attacks in only 24 per cent of cases. Tasche and Spano²⁹ reported an incidence of previous attacks of 57 per cent, but their figures included cases in which the patient was treated conservatively after perforation and returned for operation later.

PHYSIOLOGY

1 Viability of Excised Appendix—In a series of 64 appendices viability of the muscle tissue was tested immediately and at intervals after operative removal. The specimens were placed in saline solution at room temperature and then were stimulated at intervals by means

43 Warwick, M. Relationship Between Oxyuriasis and Appendicitis, Am J Clin Path 5 238-248, 1935

of a faradic current Fifty acutely inflamed appendixes were so treated, and it was noted that the very acutely inflamed and gangrenous specimens gave no muscular response to stimulation even when tested within five minutes after removal The organs with a mildly acute condition responded up to two hours after removal, and the average duration of response for the entire group of acutely diseased appendixes was 26.3 minutes In contrast to this, for 14 normal appendixes similarly treated the shortest period of response was two hours and the longest was six and one-half hours The average length of response for the normal group was three and one-half hours, or eight times as long as for the acutely diseased group These results appear to indicate that acute inflammation seriously impairs the contractile power of the musculature of the appendix and that this power is entirely lost if gangrene supervenes The consequent tissue changes which must accompany resolution of the inflammatory process account for the definite organic residual signs of appendicitis

It was noted that appendixes when stimulated tended always to bend toward the antimesenteric side, indicating that the musculature of the mesenteric side is not as well developed as that on the antimesenteric side The entering blood vessels account for part of this muscular weakness After this contraction of longitudinal muscle there was contraction of the circular muscle, the organ becoming smaller in diameter and tending to empty its lumen These contractions were very slow and lasted for several minutes The most active motion was observed near the base, and the least activity was near the tip

2 *Mechanism of Obstruction*—The effectiveness of obstruction of the appendical lumen by an impacted fecalith was tested in 2 cases, as follows The specimens were gangrenous appendixes removed at operation, in each a fecalith was impacted in the region of the base These specimens were gangrenous and showed distention distal to the obstruction, but were normal in caliber and gross appearance proximally In each instance a fine needle was introduced into the tip of the appendix, and fluid was injected into the distal portion of the lumen This caused increasing distention of the lumen, but there was no leakage around the fecalith and no fluid escaped from the unclamped base A cannula then was tied into the base, and fluid readily ran into the appendix, passed the fecalith and distended the distal portion of the lumen Solution of potassium iodide was used in the lumen and roentgenograms were taken to show the obstruction (fig 2) These experiments demonstrated that an impacted fecalith in the appendix serves as an effective ball valve, allowing ingress of fluid but preventing its escape This makes it easy to see why enemas or diarrhea subsequent to catharsis may hasten perforation of the obstructed appendix

3. *Theories of Function*—The appendix is generally considered to be a vestigial structure, without definite function. Boggian and Stellatelli,⁴⁴ however, suggested the novel theory that the appendix originates peristalsis which controls the excretory function of the large bowel, that is, when the column of fecal matter in the ascending colon reaches a sufficient weight the appendix is stimulated to contract, and this peristalsis passes the length of the large bowel, causing a desire to defecate. Proponents of this opinion have decried appendectomy as a cause of constipation. Boggian⁴⁵ found that the appendical mucosa



Fig. 2—Roentgenograms showing obstructing fecaliths in the lumens of acutely inflamed appendixes. Injections of sodium iodide were made into the lumens. In one specimen the lumen is incompletely filled. Lamination and calcification in the fecaliths are shown.

contains a water-soluble substance which stimulates gastric secretion when given by mouth. The significance of this observation is not apparent. Other concepts, mentioned by Kelly and Hurdon,⁸ are that

44 Boggian, B., and Stellatelli, M. Su di una probabile azione fisiologica dell'appendice, *Gior ven di sc med* 8 1145-1151, 1934.

45 Boggian, B. L'influenza degli estratti di mucosa appendicolare sulla secrezione gastrica, *Riforma med* 51 446-451, 1935.

the appendix secretes a special digestive enzyme specific for cellulose, that it serves to dilute the cecal content, that it secretes a lactopeptone, that it pours out a pancreatic-like juice and that it secretes a hormone. Some authors have reported dire effects on the endocrine glands subsequent to appendectomy.

The most useful observation to date on the physiologic activity of the appendix is that of Wangensteen, Buirge, Dennis and Ritchie.²⁷ They found that the human appendix, although part of an absorbing segment of bowel, actually secretes fluid at the rate of about 1 to 2 cc daily and is capable of spontaneously building up an intraluminal pressure of about 40 cm of water. This is the simplest explanation for the gradual distention and rupture of closed loops of appendix, but there are three other sources of fluid. 1. I¹⁴ have shown that hypertonic contents in the obstructed lumen attract fluid, owing to osmotic imbalance, even in the obstructed cecal appendage of the dog, which normally is an absorbing organ. Under these conditions the volume of fluid in the lumen may increase as much as six times in twenty-four hours. 2. Previously described experiments have shown that an impacted fecalith may allow ingress of fluid from the cecum but prevent its exit, the obstructing fecalith acting as a ball valve. 3. Wilkie¹⁹ has shown that bacterial decomposition of the contents of the lumen produces both fluid and gas, which distend the lumen. Protein content gives the most rapid distention, with early perforation. No doubt a combination of these factors acts to cause perforation in acute obstructive appendicitis.

PATHOGENESIS

1. *Experimental Appendicitis*—The literature on the experimental pathogenesis of acute appendicitis falls into one of two categories: that which deals with direct experimentation on the appendix or that relating to the physiologic and pathologic character of closed loops of intestine.

(a) *Direct Experimentation*. The older investigators were concerned mainly with attempting to show that organisms from the nasopharynx, when injected into the blood stream, would localize in the appendix of the experimental animal. Tedesco,⁴⁶ Kretz⁴⁷ and Adrian³⁵ injected various organisms into the tonsillar fossae of rabbits and then attempted to show appendiceal localization. They mentioned, but conveniently avoided considering, that these rabbits showed generalized lymph-

46 Tedesco, F. Experimenteller Beitrag zur Infektion der Appendix vom Rachenringaus, *Archiv für die Gesamte Anatomie und Pathologische Anatomie* 6: 111-119, 1907.

47 Kretz, R. Untersuchungen über die Ätiologie der Appendicitis. *Mitteilungen der Grenzgebiete der Medizin und Chirurgie* 17: 1-9, 1907.

adenopathy, septicemia and pneumonia. This indicates that the reaction of the appendical lymphoid tissue was only a part of the general picture of reaction to massive infection. The same criticism applies to the work of Poynton and Paine⁴⁸ and to that of Dorsey,⁴⁹ who injected streptococci intravenously into rabbits and demonstrated arthritis and appendicitis. Goeters,⁵⁰ in a series of rabbits, induced staphylococcic and streptococcic septicemia and then demonstrated the organisms in the lymph spaces of the appendix. Stoeber and Dahl⁵¹ employed similar methods and concluded that in septicemia organisms are excreted into the gastrointestinal tract. Richet and Saint-Girons⁵² obtained similar results and concluded that this constant passage of organisms through the tissues of the appendix renders it more liable to infection by organisms in the lumen.

To McMeans⁵³ goes the credit for demonstrating the fallacies in most of this work. He was able to duplicate the results in most of these experiments with bacterial injection, but obtained similar results after intravenous injection of sterile water into the rabbit. He concluded that the rabbit appendix is essentially a lymphoid organ, not comparable to the appendix of man. He also concluded that no organism is specific for appendicitis and that there is no evidence for appendical localization of organisms from the blood stream.

The work of Heile⁵⁴ is significant because he began to use dogs as experimental animals and because he first considered the importance of obstruction in the genesis of inflammation. He observed that the empty obstructed appendix showed no changes, whereas with fecal

48 Poynton, F. J., and Paine, A. Experimental Appendicitis by General Blood Infection, *Tr. M. Soc. London* **35** 243, 1912, A Further Contribution to the Study of the Etiology of Appendicitis as a Result of a Blood Infection, with Particular Reference to the Tonsils as a Primary Seat of Infection, *Lancet* **2** 439, 1912.

49 Dorsey, A. H. E. Bacteriology and Pathogenesis of Appendicitis, *Surg., Gynec. & Obst.* **50** 562-571, 1930.

50 Goeters, W. Die Beteiligung des Wurmfortsatzes bei Allgemeininfektionen, *Virchows Arch. f. path. Anat.* **291** 836-911, 1933.

51 Stoeber, H., and Dahl, W. Experimentelle hamatogene Infektion der Lymphfollikel des Appendix, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **24** 645-651, 1911.

52 Richet, C., and Saint-Girons, F. Contribution experimentale a la pathogenie des appendicites hematogenes, *Presse med.* **19** 271-272, 1911.

53 McMeans, J. W. Experimental Appendicitis, *Arch. Int. Med.* **19** 709-749 (May) 1917.

54 Heile, B. Ueber Entzündungen des Blinddarmhanges, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **39** 133-138, 1910, Ueber die Entstehung der Entzündungen am Blinddarmhang auf bakteriologischer und experimenteller Grundlage, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **26** 345-378, 1913, Die Ursache der akuten Appendicitis im Experiment, *München med. Wchnschr.* **72** 211, 1925.

material in the obstructed lumen gangrene, perforation and peritonitis resulted. Boit and Heyde⁵⁵ obtained similar results and concluded that obstruction of the lumen resulted in increased virulence of the fecal organisms. Beaussenat and Dieulafoy both found that obstruction of the appendical lumen resulted in gangrene and perforation. Eichoff and Pfannenstiel⁵⁶ found that obstruction caused gangrene, but it is significant that they were so influenced by the dictums of Aschoff⁵⁷ that they ascribed any inflammatory change to increased virulence of bacteria in the lumen due to stasis. Another criticism of this work is that the animals were allowed to die of perforation and peritonitis or the process to progress to healing. In none of this work were appendices removed at various intervals and subjected to microscopic examination.

Apparently, Van Zwalenburg⁵⁸ had the clearest insight into the problem, but his excellent papers have remained relatively obscure. He stated that simple infection does not account for the suddenness of the attack or for the early severity of the tissue changes in acute appendicitis. He stated that the evident interference with blood supply is best accounted for on the basis of obstruction and increased intraluminal pressure. He recognized that the blood supply to a sterile organ can be cut off with relative impunity for hours, whereas in the appendix serious difficulties arise because of the invasion of the dead tissue by bacteria from the lumen.

Wangensteen and I¹⁵ studied the effects of complete and incomplete obstruction, maintenance of increased intraluminal pressure, isolation of the appendix as a closed loop, the role of various bacteria, interference with circulation and a number of miscellaneous factors in an attempt to determine what factors favor the development of acute appendical inflammation experimentally. We concluded that obstruction and infection are the two most important factors and that the sequence of events is like that in obstruction of a closed loop. We observed

55 Boit, H. Ueber experimentelle Appendicitis. *Berl klin Wchnschr* **49** 812, 1912. Boit, H., and Heyde, M. Untersuchungen Experimentelles über die Aetologie des Appendicitis. *Beitr z klin Chir* **79** 271-285 1912.

56 Eichoff, E., and Pfannenstiel, W. Untersuchungen über experimentelles Appendicitis, *Beitr z klin Chir* **151** 171-202 1930.

57 Aschoff, L. Die Wurmfortsatzentzündung. Eine pathologisch-histologische und pathogenetische Studie, Jena. Gustav Fischer, 1908.

58 Van Zwalenburg, C. (a) Obstruction and Consequent Distention the Cause of Appendicitis, as Proved by Cases and by Experimental Appendicitis in Dogs, *J A M A* **42** 820-827 (March 26) 1904, (b) The Relation of Mechanical Distention to the Etiology of Appendicitis. *Ann Surg* **41** 437-450 1905. (c) Strangulation Resulting from Distention of Hollow Viscera. *ibid* **46** 780-786 1907. (d) Hydraulic Vicious Cycle in the Intestine. *Am J Surg* **18** 104-112 1932.

that the obstructed cecal apex of the dog always became inflamed unless the lumen was washed clean, and then there were no changes even after six weeks. We also found that constant intraluminal pressures up to 15 cm of water acting for six to eighteen hours produced changes in the tissues ranging from acute to gangrenous.

Recently, Wangensteen, Burge, Dennis and Ritchie²⁷ have shown that if a needle is introduced into the tip of the human appendix there is resistance to the free flow of water into the cecum. Investigations on 96 specimens showed the following degrees of water pressure to be sustained

	Average, Cm	Maximum, Cm	Minimum, Cm
Normal appendixes	38	110	16
Appendixes removed after interval	54	130	16
Acutely inflamed appendixes	73	120	12
Appendix of cadavers	3	9	0

These results indicate that even in the absence of definite organic obstruction to the lumen a considerable degree of pressure can be built up in the appendix. The same authors have shown that the appendix of man and that of the rabbit secrete fluid and so tend to distend as a closed loop. They found that the usual volume of the lumen of the appendix in man ranges between 0 and 0.3 cc. In a series of specimens the volume of the lumen at which rupture occurred was determined. The average volume was 5.8 cc, the maximum was 9 cc and the minimum was 3 cc. Gangrenous appendixes were found to rupture at a pressure of 70 cm of water, and normal appendixes at a pressure of 1,500 cm of water. They also found that if the vessels in the mesentery of an obstructed rabbit appendix were ligated no secretion into the loop occurred. Otherwise, rupture occurred in about three hours, pressures up to 72 cm of water having been built up spontaneously. Rupture could be much hastened by oral administration of croton oil or intravenous injection of hypertonic solution of sodium chloride.

(b) Indirect Evidence. The results of the foregoing investigations have led to the conclusion that the appendix may act as a closed loop. They make pertinent, therefore, a consideration of the literature bearing on this point.

Gatch⁵⁹ and Dragstedt and their associates⁶⁰ have shown that distention of the bowel reduces its blood supply and that if pressure

⁵⁹ Gatch, W. D., Trusler, H. M., and Ayers, K. D. Effects of Gascon's Distention on Obstructed Bowel. Incarceration of the Intestine by Gas Trap. Arch Surg **14** 1215-1221 (June) 1927.

⁶⁰ Dragstedt, C. A., Lang, V. P., and Millet, R. F. Relative Effects of Distention on Different Portions of Intestine, Arch Surg **18** 2257-2263 (June) 1929.

is such as to shut off the arterioles gangrene results Van Beuren⁶¹ gave this as the mechanism of perforation in intestinal obstruction Sperling⁶² and Herrin and Meek⁶³ found that obstruction is an intense secretory stimulus, and Burget and his associates⁶⁴ observed that dogs with closed loops of jejunum could be kept alive only by repeated aspiration of the contents of the loop to prevent distention, gangrene and perforation Van Zwalenburg^{58d} stated that distention increases peristalsis and secretion, which augment distention, and thus a hydraulic vicious cycle is established

Parker,⁶⁵ Banks⁶⁶ and others have shown that carcinoma of the cecum may occlude the appendical orifice and thus form a closed loop in which acute inflammatory changes develop Rost,⁶⁷ Sperling⁶⁸ and others have demonstrated that obstructing carcinoma of the sigmoid flexure of the colon may cause perforation of the cecum in the presence of a competent ileocecal sphincter, owing to distention of this closed loop These observations when applied to the appendix make it easy to understand the changes incident to the development of a closed loop It has been shown in a previous paper¹⁴ that acute and gangrenous changes may develop even in sterile organs in which increased intraluminal pressure is maintained (fig 3)

2 *Clinical Pathogenesis*—It is recognized that foreign bodies may erode the appendical wall, that infection may develop in other ways or that trauma may cause appendicitis but the following sequence of events is postulated as that which usually operates in the development of acute appendicitis^{58b}

61 Van Beuren F T Mechanism of Intestinal Perforation Due to Distention, *Ann Surg* **83** 69-78 1926

62 Sperling L Mechanics of Simple Intestinal Obstruction An Experimental Study, *Arch Surg* **36** 778-815 (May) 1938

63 Herrin R C, and Meek W I Studies in Intestinal Obstruction *Am J Physiol* **97** 532-533, 1931

64 Burget G E Martzloff K Suckow G, and Thornton R C B Closed Intestinal Loop Relation of the Intraloop (Jejunum) Pressure to the Clinical Condition of the Animal *Arch Surg* **21** 829-837 (Nov) 1930 Burget G E, Martzloff, K H Thornton R C B, and Suckow G R Closed Intestinal Loop Observations on Dogs with Jejunal and Ileal Loops and Chemical Analyses of Blood *Arch Int Med* **47** 593-600 (April) 1931

65 Parker, G E and Rosenthal D B Carcinoma of the Large Bowel as the Direct Cause of Acute Appendicitis and Simultaneous Acute Intestinal Obstruction *Lancet* **2** 1089-1090, 1933

66 Banks A G, and Green R D Acute Appendicitis Associated with Carcinoma of the Cecum *Brit M J* **1** 926 1935

67 Rost F Pathological Physiology of Surgical Diseases Philadelphia P Blakiston's Son & Co 1923 p 222

68 Sperling, L Role of the Ileocecal Sphincter in Cases of Obstruction of the Large Bowel, *Arch Surg* **32** 22-48 (Jan) 1906

(a) Probable Sequence of Events The lumen of the appendix becomes occluded by a slowly enlarging fecalith or by some other mechanism, and a closed loop is thus formed. Peristalsis is stimulated as the appendix attempts to overcome the obstruction, and the patient notices cramplike pains in the abdomen. The peristalsis, together with the obstruction acts as a secretory stimulus, and the lumen gradually fills with fluid from this source and also from the action of bacteria on its contents. The distention causes pressure on the terminations of the sympathetic nerves, and the patient experiences pain, of a more

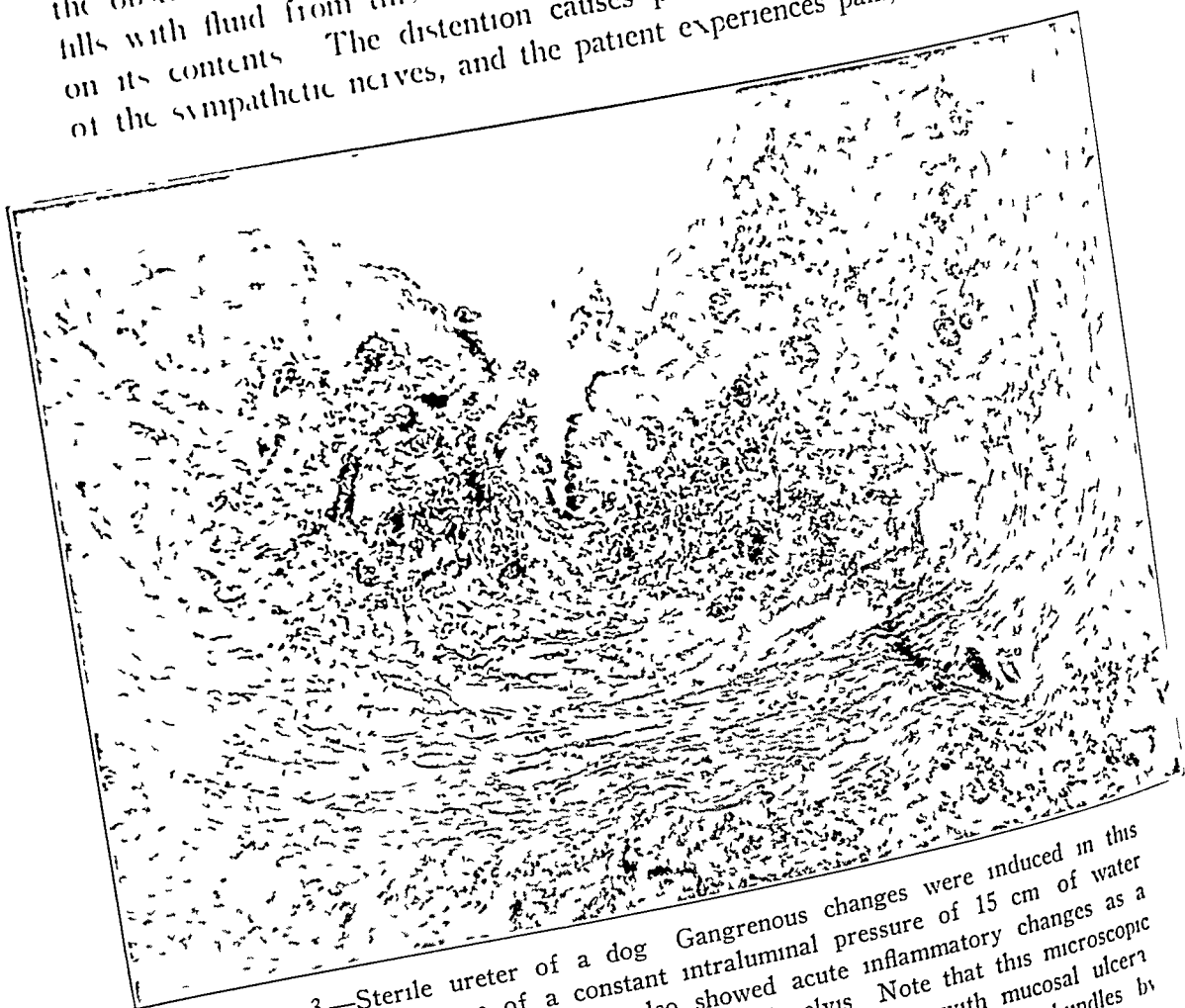


Fig 3—Sterile ureter of a dog. Gangrenous changes were induced in this ureter by maintenance of a constant intraluminal pressure of 15 cm of water for eighteen hours. The kidney also showed acute inflammatory changes as a result of the pressure within the sterile renal pelvis. Note that this microscopic picture closely resembles that seen in severe appendicitis, with mucosal ulceration, dense infiltration with leukocytes and separation of muscle bundles by accumulation of inflammatory exudate.

constant nature and usually referred to the umbilical region. As distention increases, the capillaries and venules become occluded, while in the arterioles blood continues to be pumped in at systolic pressure.

Vascular congestion follows, and edema and diapedesis of leukocytes begin. The distention has now reached such proportions that reflex nausea and vomiting occur, and the patient has such severe pain that it is recognized as coming from the right lower quadrant of the abdomen. Distention progresses, and inflammatory reaction increases until the terminations of the visceral afferent nerves are killed by pressure or by anoxemia. The pain then becomes less. The distention now has completely shut off the capillaries and smaller veins so that thrombosis occurs. The antimesenteric border has the poorest blood supply, here diamond-shaped infarcts develop first. The reaction has now reached the serosa so that the patient experiences pain from a peritoneal source and rebound tenderness with rigidity can be elicited. As more blood is pumped into the appendix the smaller vessels rupture, and hemorrhage occurs. By this time the walls distal to the obstruction are thinned by distention, and the mucosa has become ulcerated and destroyed as a result of pressure necrosis. Fever, rapid pulse and leukocytosis have developed as a consequence of absorption of dead tissue products. As soon as necrosis of tissue appears bacteria may enter the tissues. If the appendix is not able to overcome the obstructing mechanism⁷⁰ perforation eventuates, usually through one of the infarcted areas on the antimesenteric border. At this stage the patient experiences relief of pain, due to release of pressure. Westphal²² suggested that anaerobes form gas in the lumen and that perforation is in the nature of an explosion.

(b) Cause of Regression. The appendicitis may regress spontaneously if the appendix can expel the fecalith, overcome any other type of obstruction which may be present or dissolve the fecalith. Ochsner⁷⁰ stated that he had several times found the fecalith just escaping into the cecum, owing to relaxation caused by the anesthetic. He also had found fecaliths in the cecum evidently just expelled. Ochsner also saw appendices distended by gas and obstructed at the base by spasm. In this series it frequently has been noticed that with long duration of the disease the fecalith becomes soft and tends to disintegrate. Some were recognized by the marked depression left in the mucosa at the site of obstruction, and others were identified by concentrically placed masses of calcareous material on roentgen examination. The possibility of neurogenic spasm or anomaly of the sphincter at the appendiceal base has not been considered in this investigation.

(c) Effect of Catharsis on Perforation. Catharsis long has been known to favor perforation in appendicitis. Schmidt⁷¹ showed a

⁷⁰ Ochsner, A. I. *A Handbook of Appendicitis*. Chicago: G. P. Engelhard & Co., 1902.

⁷¹ Schmidt, cited by Egdahl.²⁰

postcathartic mortality of 86 per cent as compared with a total mortality of 5 and 12 per cent for primary appendicitis without rupture. It may be that one bad effect of the cathartic is simply that the patient delays consulting a physician until the cathartic has had an opportunity to act, but it seems more likely, from experimental evidence, that the cathartic stimulates peristalsis and secretion, thus hastening perforation of the obstructed appendix. Enemas also may cause perforation by overdistention of the appendix. In this connection it should be stated that the various diagnostic tests which depend on back pressure into the appendix to cause pain should be avoided because of the possibility of traumatic perforation of the viscus (fig 4).

(d) Experimental Recapitulation. In order to test the foregoing theory of pathogenesis, 3 patients in the "interval" group were operated



Fig 4—Changes in the appendical wall and lumen incident to obstruction. The position of the obstructing fecalith is shown, and it will be noted that distal to this point the lumen is dilated, the mucosa is sloughing, the wall is very thin and the mesenteric vessels are thrombosed. Proximal to the obstruction the lumen is of normal caliber and the wall is of ordinary thickness.

on with the region under local anesthesia. The cecum was delivered onto the abdominal wall, and the base of the appendix was ligated. This procedure caused the patient no pain. A fine needle was then introduced into the appendical lumen through the tip, and saline solution was introduced gradually through a syringe. In 1 patient moderate distention caused marked blanching of the organ, and with progressive distention the decrease in circulation could be visualized. This patient had severe generalized abdominal pain, which was abolished by cutting the mesoappendix. Some fluid was transuded through the appendical wall, this may indicate in part the formation of peritoneal fluid. In a second patient a similar procedure was carried out, and it was found that an acute pressure of 125 cm. of water in the appendix did not

cause pain because the musculature contracted violently and there was no distention. When the syringe was used and saline solution was injected slowly over a period of minutes, 6 cc caused emptying of the vessels along the antimesenteric border, the walls became thinned, owing to distention, and fluid was exuded. The patient had generalized abdominal pain, and with increased distention this pain localized in the right lower quadrant. After the saline solution was aspirated from the lumen the appendix contracted and became hyperemic, but remained 1.5 cm longer than before distention. The lumen was distended again, and the pain was relieved by cutting the mesoappendix. In the third patient, similarly prepared, slow distention caused vague abdominal discomfort, followed by pain in the right lower quadrant and nausea. These symptoms were relieved by aspirating the solution or cutting the mesoappendix. The patient said that this procedure caused symptoms closely simulating those of previous spontaneous attacks which had been diagnosed as acute appendicitis.

BACTERIOLOGY

According to the obstructive theory of the origin of appendicitis, bacteria are purely secondary to mechanical factors in the majority of cases. Nevertheless, it was felt advisable to conduct investigations with regard to the flora of the appendixes in this series.

1 *Postmortem Changes*—In reviewing the literature it was found that some authors stated that appendixes removed at emergency operation during the night were placed in the ice box until morning, when material was taken for culture. It was my thought that postmortem invasion might account for many of the cultures yielding bacteria in such cases, the following experiment, therefore, was carried out. In 8 cases the operatively excised appendix was placed in saline solution at room temperature. A cross section of the organ was taken at the tip and placed in solution of formaldehyde. These appendixes were allowed to remain in the saline solution, and contiguous sections were removed and fixed after intervals ranging from five to twenty-four hours. Results in sections prepared with the Gram stain (table 3) are shown in the table.

The postmortem bacterial invaders tended to occur in rather large clumps and were not surrounded by any tissue reaction. The foregoing experiment shows the necessity of taking material for culture immediately after excision of the appendix.

2 *Clinical Bacterial Studies*—From 30 appendixes (10 from patients with interval appendectomies, 10 from patients with acute appendicitis and 10 from patients with gangrene of the appendix) cultures of peritoneal fluid of the contents of the distal and proximal

portions of the lumen and of a segment of serosa and muscularis from the distal portion were taken at the operating table. This material was incubated in liver-peptone broth, and if it was sterile after seventy-two hours no further investigation was carried out. After twenty-four hours smears of the cultures were made and stained by the Gram method. If gram-positive rods were found, milk tubes were inoculated and read for proteolytic and gas-forming organisms. The liver-peptone cultures were planted on eosin-methylene blue and blood agar plates. After twenty-four hours these plates were read for streptococci and colon organisms, and the latter were differentiated according to fermentation reactions.

TABLE 3.—*Correlation* Between the Number of Bacterial Colonies in the Tissues and the Length of Time Elapsing Between Excision of the Appendix and Preparation of the Material for Bacteriologic Study*

Case No	Fixation of First Section	Result	Time of Fixation of Second Section After Removal	Result
1	On removal	Few colonies in submucosa	5 hr later	No definite increase in colonies
2	On removal	No bacteria in tissues	16 hr later	Many colonies in all tissue layers
3	On removal	No bacteria in tissues	16 hr later	Many colonies in all tissue layers
4	On removal	No bacteria in tissues	24 hr later	Extremely numerous bacterial colonies
5	On removal	Few clumps of bacteria	24 hr later	Apparently fewer than in early fixation
6	On removal	No bacteria in tissues	24 hr later	Many colonies in all layers
7	1 hr after removal	No bacteria in tissues	24 hr later	Many colonies in all layers
8	1 hr after removal	Few colonies in submucosa	24 hr later	Dense infiltrating clumps of bacteria

* This relation is proof that in order to eliminate error one should prepare the material for study immediately after removal of the appendix.

In these 30 cases a direct correlation was found between the severity of the disease and the presence of bacteria in the tissues. The culture method revealed bacteria in the following percentage of cases

	Appendectomy After Interval	Acute Appendicitis	Gangrene
Tissue	0	20%	60%
Peritoneum	20%	10%	0
Lumen	90%	100%	100%

The 20 per cent incidence of bacteria in the peritoneal cavity in the cases of interval appendectomies is due to the fact that in these cases there was a residual abscess from the previous perforation. In the same group one lumen was sterile, but this was a mucocoele.

Comparison of Tissue Gram Stain and Culture Methods—There seems to be a general feeling among pathologists that the method

of demonstrating bacteria by staining tissues with Gram's stain is not reliable. In this series there was an excellent opportunity to evaluate this idea, for the two methods were used simultaneously and were checked against each other. The percentage of cases in which the results were positive are compared for the two methods as follows:

	Acute Appendicitis	Gangrene	Appendectomy After Interval	Gynecologic Group	Experimental Series
Gram tissue stain	21%	63%	2%	21%	19%
Culture method	27%	60%	0		

It is interesting to note that in each group the Gram tissue stain gave a slightly higher percentage of positive results than the culture method.

The various types of organisms and the frequency with which each occurred, as shown by the culture method, were as follows:

	Bacillus Coli Communis	Bac- terium Coli Communior	Bacillus Aerog- enes	Strepto- coccus Haemo- lyticus	Staphylo- coccus	Proteo- lytic Aerobe	Clos- tridium Welchii
Tissue	1%	7%	3%	3%	7%	7%	0
Peritoneum	7%	0	0	3%	0	0	0
Distal part of lumen	7%	3%	3%	0	0	7%	3%
Proximal part of lumen	27%	27%	20%	3%	0	13%	3%

The gram-positive diplococci described by Aschoff and also by Gundel and his associates¹² were not observed in this investigation. This is the usual experience of American authors. The incidence of mixed organisms in this series, as shown by the culture method, was as follows:

	1 Organism	2 Organisms	3 Organisms
Tissue	10%	17%	0
Peritoneum	3%	3%	0
Distal part of lumen	0	6%	3%
Proximal part of lumen	30%	23%	6%

It is interesting to note that the lumens of normal appendices appeared to contain more organisms than did those of inflamed appendices. This observation has been made by other investigators but no especial significance can be attached to it, as it may be simply a phenomenon of dilution.

In 17 per cent of cases of acute appendicitis due to obstruction, bacteria were present in the tissues, as compared with 9 per cent in the group in which no obstruction was present. This agrees with the results in the experimental series¹⁵ and probably means that increased intraluminal pressure in the presence of obstruction forces bacteria into the tissues.

72 Gundel M. Ueber die Erregerfrage bei der Appendicitis und post-appendicularen Peritonitis. Arch f klin Chir **172** 597-623 1933. Gundel M. Paget W. and Sussbrich F. Untersuchungen zur Aetiologie der Appendicitis und post-appendicularen Peritonitis. Beitr z path Anat u z allg Path **91** 300 438 1933.

4 *Bacteria in Appendicular Peritonitis*—In the Minneapolis General Hospital series, 11 cases of appendicitis with perforation and peritonitis were studied with reference to the bacterial content of the peritoneal exudate. Bacteria were found in the peritoneum in 81 per cent of cases. In 36 per cent of cases there was only one type of organism, in 27 per cent there were two types, in 9 per cent there were three types, and in 9 per cent there were four types. The following organisms were isolated. The incidence of each was as follows:

	Incidence, %
<i>B. coli</i> communis	45
<i>Bact. coli</i> communior	45
<i>Enterococcus</i>	27
<i>Streptococcus</i>	18
<i>Bacillus fusiformis</i>	9
<i>Diphtheroids</i>	9

Twelve cases of nonperforative appendicitis in the same series were similarly studied, in only 16 per cent were there bacteria in the peritoneal cavity. *Bact. coli* communior was isolated in 1 case and *Streptococcus viridans* in another.

5 *Review of Literature*—In the general enthusiasm over the theory of the bacterial causation of disease, mechanical factors were forced into the background, where they have remained to this day, largely owing to the writings of Aschoff and others, who postulated a specific bacterial cause for appendicitis and all other diseases. Rosenow,⁷³ in 1915, obtained cultures yielding bacteria from the walls of 17 of 18 acutely diseased appendixes. The organisms usually were *B. coli* and *Streptococcus viridans*. These organisms when injected intravenously into rabbits were said to have resulted in acute appendicitis. The previously cited work of McMeans⁵³ threw doubt on these results, however. In 1921, Rosenow⁷⁴ went so far as to state that organisms isolated in cases of peptic ulcer, cholecystitis, appendicitis and pancreatitis produced similar lesions when injected intravenously into experimental animals. His enthusiasm for the theory of elective localization of bacteria has not been generally shared.

In 1925, Warren⁷⁵ studied a series of acutely diseased appendixes by gram-stained sections and by cultures of the serosa and muscularis. He observed all early lesions to be located at the margins of the lumen, an observation which he interpreted as evidence against the hematogenous route of infection. Warren was not able to demonstrate the organism described by Aschoff, and he concluded that appendicitis is

⁷³ Rosenow, E. C. Bacteriology of Acute Appendicitis, *J. Infect. Dis.* 16: 240-268, 1915.

⁷⁴ Rosenow, E. C. Focal Infection and Elective Localization of Bacteria, *Surg., Gynec. & Obst.* 33: 19-26, 1921.

⁷⁵ Warren, S. Etiology of Acute Appendicitis, *Am. J. Path.* 1: 241-246, 1927.

not a specific bacterial disease. In a series of 288 cases he found *B. coli* alone in 57 per cent, *B. coli* and streptococci in 19 per cent and streptococci alone in 8 per cent.

The idea that organisms swallowed from the throat may set up appendical inflammation has intrigued many investigators. Hilgermann and Pohl⁷⁶ presented the following figures in this regard:

Organism	Single Organism			Combined with Other Organisms	
	Throat and Appendix	Throat	Appendix	Appendix	Throat
<i>Pneumococcus</i>	56%	19%	4%	60%	75%
<i>Streptococcus</i>	21%	33%	5%	32%	64%
<i>Diphtheroid</i>	7%	1%	3%	10%	8%
<i>Staphylococcus</i>	13%	19%	0	14%	32%
<i>Vincent's bacillus</i>	0%	1%	0	11%	10%

Gundel⁷² stated that he had isolated the same strain of pneumococci from the throat and from the appendix in a series of cases and he postulated primary pneumococcic infection with secondary invasion by putrefactive and colon bacilli. All blood cultures were sterile. Gundel found that most inflamed appendixes did not show intestinal flora. In 27 of 31 cases he isolated a gram-positive diplococcus, and in 10 of 15 cases the same organism was seen in microscopic sections. He found the same organism to be the one most frequently phagocytosed and most frequently isolated from the pus of appendical abscesses. From these observations Gundel concluded that a gram-positive diplococcus is the most frequent cause of appendicitis. The usual fecal type of flora could be isolated in cases of so-called chronic appendicitis.

Meleney, Harvey and Jern,⁷⁷ in an excellent paper, reported that the incidence of anaerobes was less than 50 per cent in cases of perforative appendicitis and that these organisms were scarce in cases of gangrene of the appendix. They concluded that gangrene is vascular rather than bacterial in origin. In no case did death occur in the absence of perforation, even though several organisms could be cultured from the peritoneal fluid.

Cazzamali and Miglierina⁷⁸ concluded that the peritoneal fluid in cases of early appendical peritonitis is apt to be sterile but in the late stage of the disease is polymicrobial. They found that anaerobes traverse the appendical wall with difficulty in the absence of perforation.

76 Hilgermann R, and Pohl W. Beitrag zur Aetiologie und Serumtherapie der foudroyanten Appendicitis auf Grund der Beobachtungen bei 300 Fällen im Kreise Deutsch-Krone. Arch f klin Chir **154** 248-319 1929.

77 Meleney, F L. Harvey H D and Jern H Z. Peritonitis. Correlation of the Bacteriology of the Peritoneal Exudate and the Clinical Course of the Disease in One Hundred and Six Cases of Peritonitis. Arch Surg **22** 1-66 (Jan) 1931.

78 Cazzamali, P and Miglierina R. La batteriologia delle peritoniti acute. Arch ital di chir **34** 573 675 1933.

Recently, Collins⁷⁹ has investigated the bacteriologic features of chronic appendicitis. In a total series of 209 cases he obtained tissue cultures yielding bacteria in 16.2 per cent. All of the totally obliterated appendixes were sterile, but 47 per cent of the cultures yielding bacteria were of tissue from partially obliterated appendixes.

The results of this investigation and those of the work of most other authors indicate that appendicitis is not specifically a bacterial disease. The results of this investigation seem to indicate that bacteria appear late or not at all in the course of appendicitis and therefore play a secondary role in the causation.

PATHOLOGY

1 *Mortality*—Tasche and Spano⁸⁰ reported a mortality rate (1922 to 1930) of 3.4 per cent for a series of 700 cases, while Sperling and

TABLE 4—*Mortality Rate in the Present Series**

	Cases		Deaths		Mortality, Percentage	
	Minneapolis General Hospital	University Hospitals	Minneapolis General Hospital	University Hospitals	Minneapolis General Hospital	University Hospitals
Interval appendectomy	16	131	0	0	0	0
Acute appendicitis	49	43	0	0	0	0
Gangrene	20	57	0	0	16.66	0
Perforation and local peritonitis	12	4	2	0	9.09	0
Perforation and general peritonitis	22	0	2	0		0
Total	119	235	4	0	11.76	0
Nonperforative acute appendicitis	69	100	0	0	0	0
Perforative appendicitis	34	4	4	0	11.76	0

* The Minneapolis General Hospital series includes all appendixes removed at that institution in 1935. The University Hospitals series includes all appendixes removed there in 1935. Cases in which no operation was done have not been included in this study.

Myrick⁸⁰ reported a rate of 5.6 per cent for 518 cases observed subsequently (1932 to 1935) at the same hospital. The mortality rate in this series is shown in table 4. There was a total mortality of 1.08 per cent for the entire series.

2 *Cause of Death*—Peritonitis is the usual cause of death, but in this series it did not enter into the picture. Of the 4 fatalities, 1 patient died of pulmonary embolism on the eighth postoperative day. Another died of cerebral hemorrhage and pneumonia on the thirtieth postoperative day. The third died of mastoiditis, thrombosis of the

⁷⁹ Collins, D. C. Bacteriologic Studies of Chronic Appendicitis, *Ann Surg* 103: 870-874, 1936.

⁸⁰ Sperling, L., and Myrick, J. C. Acute Appendicitis. Review of Five Hundred and Eighteen Cases in University of Minnesota Hospitals from 1932 to 1935, *Surgery* 1: 255-264, 1937.

lateral sinus and septicemia more than a month after appendectomy, and the fourth had scarlet fever on the eighth postoperative day, followed by pneumonia, septicemia and death more than a month after appendectomy. In a study of 1,000 cases of fatal peritonitis, Pflaum⁸¹ found appendicitis to rank second as the cause of peritonitis, being responsible in 12.6 per cent of cases.

3 *Obstruction*—The incidence of definite luminal obstruction in the present series was 80 per cent and the distribution among the groups was as follows:

	Acute Appendicitis	Gangrene	Localized Peritonitis	Generalized Peritonitis	Colic	Appendectomy After Interval	Parasites	Gynecologic Group
Minneapolis General Hospital	75%	90%	100%	95%	100%	37%	0	
University Hospitals	25%	84%	100%			20%	57%	3%
Total	40%	87%	100%	95%	100%	28%	22%	3%

The obstruction was an impacted fecalith in 67 per cent of cases, and other factors operated in the following number of instances (fig. 5):

Obstruction	Acute Appendicitis	Gangrene	Appendectomy After Interval
Anatomic position	1	5	4
Inspissated feces	2	2	5
Polyyps	1	1	2

This classification does not include the organic residual signs of previous appendicitis, which will be discussed under another caption (fig. 6).

The patients in the pediatric age group (up to 16 years) were studied as to the presence of obstruction and incidence of fecaliths. It was found that for the pediatric groups the incidence of obstruction was about 5 per cent greater than for the adults and the incidence of fecaliths was about 10 per cent greater than for the adults.

	Acute Appendicitis				Gangrene				Perforative Appendicitis			
	Obstruction		Stone		Obstruction		Stone		Obstruction		Stone	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Pediatric group	9	38	12	46	18	90	14	74	11	100	9	90
Adult group	35	53	22	34	48	83	3	63	23	95	23	82

4 *Increased Intraluminal Pressure*—The incidence of increased intraluminal pressure as evidenced by distention of the lumen and flattening of the mucosal folds is fairly closely correlated with the presence of obstruction. In most cases incision of the appendical wall caused the contents to be forcibly ejected. That flattening of the mucosa results from intraluminal distention was shown by fixing normal appendices with their lumens distended by saline solution. These appendices showed flattening and desquamation of epithelium similar

81 Pflaum C C. A Postmortem Analysis as to Etiology in One Thousand Cases of Peritonitis, *Am J Clin Path* 5:131-150, 1935.

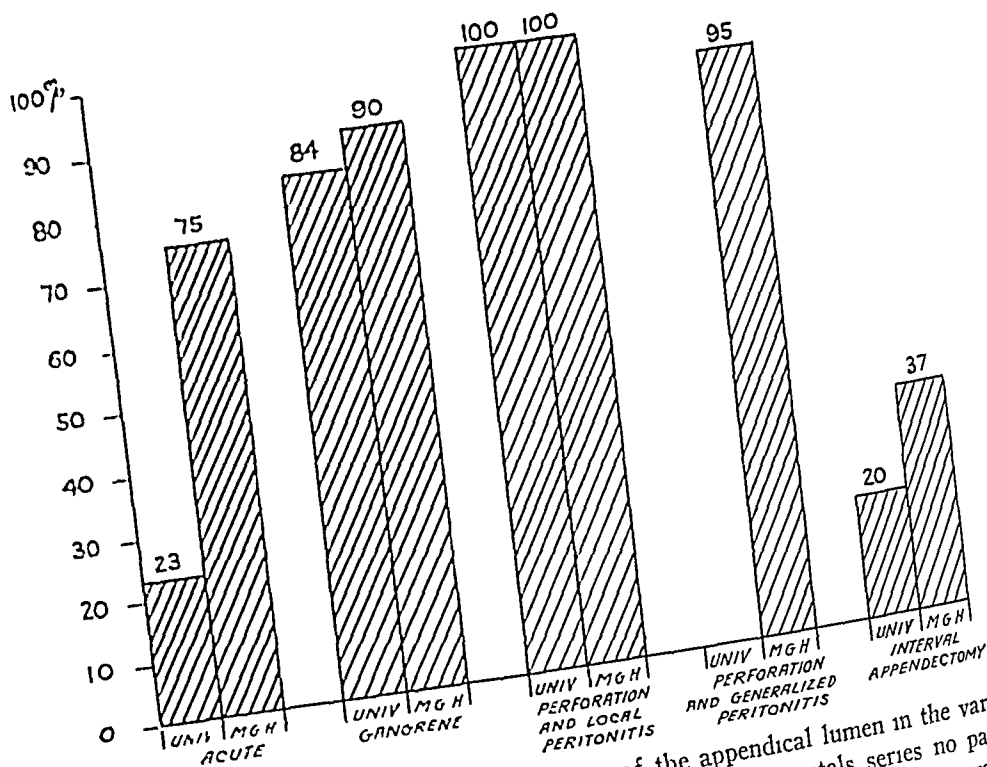


Fig 5—Incidence of organic obstruction of the appendical lumen in the various types of appendicitis in this series. In the University Hospitals series no patient with perforation and generalized peritonitis was subjected to primary operation. Such patients were treated conservatively, and the appendix was removed after about six weeks.

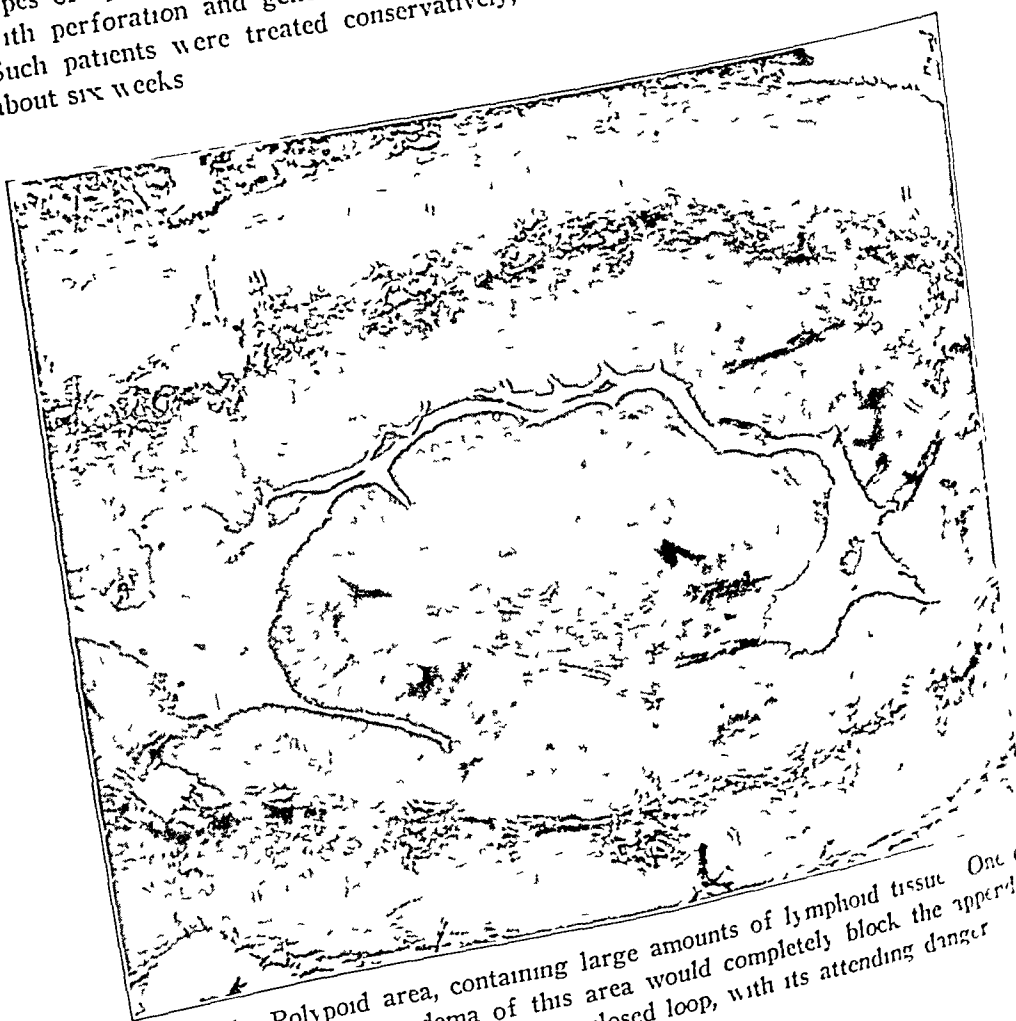


Fig 6—Polypoid area, containing large amounts of lymphoid tissue. One can see readily how slight edema of this area would completely block the appendiceal lumen and lead to the formation of a closed loop, with its attending danger.

to the changes seen in acute appendicitis. The incidence of increased intraluminal pressure in this series was as follows:

	Acute Appendicitis		Gangrene		Localized Peritonitis		Generalized Peritonitis		Colic		Appendectomy After Interval		Gynecologic Group	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Minneapolis General Hospital	32	65	20	100	10	51	12	54	4	80	1	7		
University Hospitals	6	15	36	63	4	100					20	15	1	3
Total		40		51		90		54		80		11		3

Release of pressure by perforation is the obvious reason for the smaller incidence of demonstrable pressure in the cases in which perforation and peritonitis were present.

In this series 2 appendices showed diverticula. These pouches contained fecaliths and evidently had been formed as the appendix attempted to expel the concretion. On section these pouches were seen to contain no muscle fibers in their walls.

Williams and Boggon⁸² observed obstruction of the lumen in 97.2 per cent of a consecutive series of 108 acutely diseased appendices and noted that inflammation was confined to the obstructed area. Diverticula distal to the obstruction were found in 6 cases. Edwards⁸³ observed 8 cases of diverticula in 1,493 appendices. The diverticula were multiple in all instances and were seen in cases in which there was stenosis of the lumen at the base of the appendix. Edwards concluded that these pouches develop as a result of increased intraluminal pressure, but he did not suggest that the pressure may cause appendicitis. These pouches were most often seen on the mesenteric side, where the muscle layer is weakened by the vascular hiatuses.

5 Incidence of Recurrence—Such microscopic observations as fibrosis of the submucosal and muscular layers, abnormal irregular thickening and vascularity of the serosa and foci of lymphocytes or plasma cells throughout the tissues have been taken as evidence of previous acute inflammation. These changes had the following incidence in this series:

	Acute Appendicitis		Gangrene		Localized Peritonitis		Generalized Peritonitis		Appendectomy After Interval		Parasites		Gynecologic Group	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Minneapolis General Hospital	17	36	5	25	0	0	4	18	16	100	1	20	5	17
University Hospital	11	25	6	10	1	25			110	91		5	17	0
Total		30		17		17		1		9		2		25

82 Williams B W and Boggon R H. Mechanics of Appendicitis. *Lancet* 1 9-10, 1934.

83 Edwards H C. Diverticula of the Appendix. *Brit J Surg* 22 88 107 1934.

These figures are much lower than those for cases in which there is a history of previous attacks, but show the same tendency toward more attacks in cases of the less severe grades of appendicitis. It should be mentioned that the figures for the gynecologic group are not particularly significant, since the group was not made up of unselected material. The appendixes usually were removed because of some appearance of gross deviation from the normal.

6 Chronic Appendicitis and Appendical Colic—From the severe changes in the muscle layer in the cases of appendectomy after an interval, as studied by the azocarmine stain, it was concluded that normal function would be impossible, and it was postulated that the repeated mild attacks of pain making up the syndrome usually called chronic appendicitis may have a basis of muscular dysfunction and colic. To test this idea, 4 of the patients in this group were operated on with the region under local anesthesia. In each case the cecum was delivered onto the abdominal wall and the patient was observed to be comfortable. The appendix then was stimulated by means of a faradic current. This resulted in marked contraction and spasm of the appendix, causing severe pain in the right lower quadrant. The appendix became white from the extreme degree of contraction. The patients thought that this simulated the attacks for which they had come to the hospital.

Aschoff⁸⁷ stated that 80 per cent of patients show microscopic evidence of previous appendicitis by the fifth decade of life. According to Cutler,⁸⁴ Williams and Boggon,⁸² Boyd⁸⁵ and others, repeated attacks of appendicitis convert the submucosa into dense fibrous tissue (fig 7). This fibrous tissue also invades the muscularis and breaks up the muscle bundles into isolated strands. The serosa becomes markedly thickened, more vascular and infiltrated with lymphocytes and plasma cells, together with new fibrous tissue. Cutler⁸⁴ stated that disturbed function rather than inflammatory change is the most constant evidence of recurrent appendicitis. It seems possible that the residual fibrosis produces enough muscular dysfunction to cause recurrent mild attacks of pain—so-called chronic appendicitis. Cole⁸⁶ stated that dysfunctioning or chronically diseased appendixes cause recurring attacks of pain in the right lower quadrant which does not radiate and is not accompanied by signs of acute inflammation. Bigelow⁸⁷ operated

84 Cutler, O. I. Mild Acute Appendicitis. Appendical Obstruction, *Arch Surg* **31** 729-741 (Nov.) 1935

85 Boyd, W. Surgical Pathology, Philadelphia, W. B. Saunders Company 1929, pp 362-381

86 Cole, W. H. Differential Diagnosis and Treatment of Chronic Appendicitis, *J. A. M. A.* **105** 147 (July 13) 1935

87 Bigelow, W. A. Study of Right-Sided Pain in So-Called Chronic Appendicitis, *Canad. M. A. J.* **23** 22-23, 1930

on patients with chronic appendicitis with the region under local anesthesia and found that pinching the appendix was followed in two or three minutes by spasm and typical severe cramplike pains. Pulling on the mesoappendix caused localized pain in the region of the appendix. Gargano⁸⁸ made an observation which correlates well with these ideas. He examined appendices by polarized light and found that in chronic appendicitis the musculature does not exhibit double refractility, which is characteristic of normal muscle. This indicates an incomplete return to normal after acute inflammation.

7 Microscopic Picture—A study of the pathologic changes in appendicitis is complicated by the fact that pathologists divide the disease arbitrarily into several types and speak of each as a definite entity. This

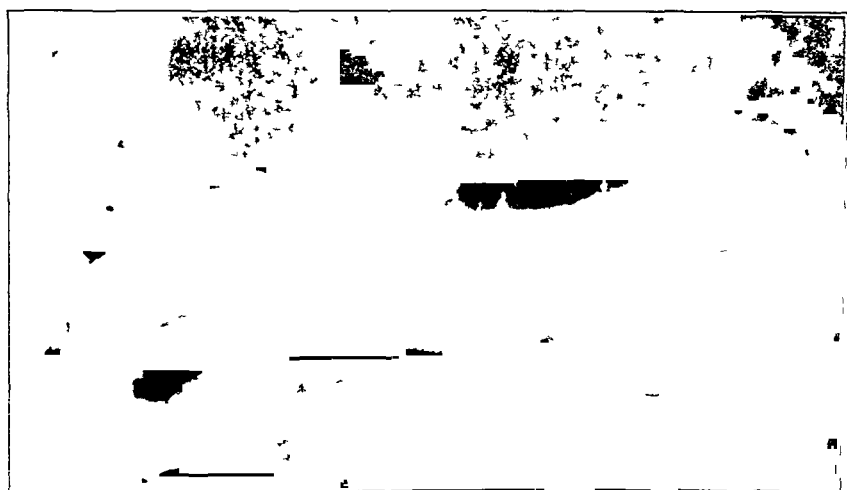


Fig 7—Appendix removed six weeks after an attack of acute appendicitis, which was treated conservatively. The gross specimen shows obliteration of the lumen in the distal fifth of the appendix. The area of dilatation contained a small fecalith. The white submucosa in this area was fibrotic on section.

attitude has led to the use of such terms as 'catarrhal appendicitis', 'suppurative appendicitis', and 'gangrene of the appendix' without regard to the fact that the disease is progressive and passes through a gradual series of changes culminating in gangrene and perforation unless the infection is controlled or the obstruction is overcome. The microscopic picture in any given case of appendicitis simply indicates the point to which the disease has advanced before being arrested by the surgeon.

The lumen on microscopic section gives valuable information not only by its size and contour but by its content. A diagnosis of

⁸⁸ Gargano, cited by Kelly and Hurdon.

obstruction can be made from examination of the section under low magnification, for dilatation of the lumen distal to the point of obstruction is invariably present whereas the lumen proximally is normal in caliber. If a fecalith has been the cause of obstruction an area of flattened mucosa is seen at the point of its impaction. The contents of the obstructed appendix are always fluid, as is true of obstructions elsewhere in the intestinal tract. The contents are made up of cellular exudate, bacteria and liquefied feces containing masses of cellulose, and in the presence of obstruction due to a fecalith there are flecks of calcareous material in the liquid content of the distal portion. In cases in which the condition is not due to obstruction the lumen is uniform in diameter, there being no dilatation in the absence of obstruction. The contents tend to be more purulent, and the fecal material, if present, may be solid. In appendixes removed after an interval of treatment the lumen is apt to contain inspissated masses of fecal matter, owing to the muscular dysfunction. Strictures and minor irregularities of the lumen are common as a result of patchy fibrosis in healing.

The mucosa has been studied incompletely by investigators, so that the normal histologic picture is not a matter of agreement among pathologists. For this reason there is much confusion arising from its examination in cases of appendicitis. Normally the mucosal layer is packed with lymphocytes, eosinophils and an occasional neutrophil. In cases in which obstruction is present, owing to the very small caliber of the mucosal vessels, distention early produces pressure necrosis. Sections through distended appendixes show flattening, thinning and patchy sloughing of the mucosa distal to the obstruction, while proximally the mucosa is of normal thickness. It is true that the area immediately surrounding the fecalith may show the greatest pressure necrosis, but the perforation rarely is seen at a point over the fecalith. The theory held by the German school is that pressure necrosis causes perforation, but this mechanism was found to operate in only 2 cases in this series. As soon as there is patchy desquamation of mucosa due to pressure, submucosal tissue is exposed to bacterial invasion, and a heavy cellular exudate develops at this point. This may be what German authors (Schrumpf⁸⁹, Noll⁹⁰) have described as a pseudodiphtheritic type of membrane in cases of appendicitis. In the nonobstructive type of appendicitis a mucosal lesion is presupposed as a precursor to bacterial invasion, but, as Aschoff admitted, it usually is impossible to demonstrate. In this series such a lesion was shown in 1 instance, in which

89 Schrumpf, P. Beiträge zur pathologischen Anatomie der Wurmfortsätzekrankungen, Mitt. d. Grenzgeb. d. Med. u. Chir. **17** 167-209, 1907.

90 Noll, R. Die Histologie der Wurmfortsatzentzündung, Mitt. d. Grenzgeb. d. Med. u. Chir. **17** 249-348, 1907.

there was mucosal ulceration at the point where a sharp spicule of bone in the lumen pierced the appendical wall. In the other cases neutrophilic infiltration was the only significant change. In the cases of appendectomy after an interval no uniform mucosal changes could be demonstrated. Areas of mucosal denudation tend to heal by obliteration of the lumen in that region so that small cystic areas frequently are seen at a later date. In some cases the appendix is represented by a fibrous cord and a small terminal cyst. Healing by fibrosis results in irregular contractures with distortion of the lumen. Spencer⁹¹ found 75 per cent of acutely diseased appendices to be bent as a result of fibrosis. In some cases the reaction may be extremely cellular so that the mucosa becomes hyperplastic and is thrown into abnormally thick folds.

The submucosa, since it carries most of the larger vessels, is important in the development of acute inflammation. There has been considerable discussion as to the site of origin of the initial lesion in appendicitis, but it is obvious that the cellular exudate must reach the appendix by way of the blood stream, so that the most vascular layer will first show accumulation of fluid and neutrophils. In addition to being most vascular, the submucosa normally is composed of a loose connective tissue stroma, which lends itself to accumulation of fluid and cells. In the early stages of appendicitis the submucosa may be the first layer to show edema and neutrophilic infiltration, which begin around the walls of vessels. Margination of leukocytes in the vessels due to vascular stasis coincident to obstruction, is also seen. These changes are most prominent and widespread in cases in which the disease is due to obstruction, for in cases in which bacteria play a part there is one focus about which inflammation centers while in the presence of obstruction all tissue distal to the obstruction shares about equally in the developing inflammation. Usually this picture was clearly evident but in some cases it was obscured by the normal accumulation of lymphoid tissue in the submucosa. In cases of appendectomy after an interval, as has been mentioned the submucosa showed infiltration with lymphocytes, eosinophils, plasma cells and new connective tissue cells. In some instances the layer was extremely fibrotic and by the use of special stains collars of lymphocytes and fibroblasts could be seen around the submucosal vessels.

The lymphoid tissue usually shares but little in the changes incident to the development of acute inflammation. In this series both in normal appendices and in appendices removed after an interval the lumen frequently was filled with lymphocytes, it was concluded therefore

91 Spencer A. M. Aetiology of Acute Appendicitis *Brit M J* 1 227-230 1938

that the lymphoid follicles periodically discharge their contents into the lumen. This belief has been shared by Thompson,⁹² who demonstrated it in the exteriorized appendixes of rabbits. This periodic rupture may allow bacterial invasion, and Schrumph⁶⁹ observed abscesses of the lymph follicles in cases of so-called catarrhal appendicitis. Noll⁹⁰ also cited this etiologic mechanism. It was observed once in this series. In cases of appendicitis due to obstruction there were no definite changes in the lymphoid tissue. In the series of cases of appendectomy after treatment, the lymphoid tissue usually was much decreased, probably as a result of the contracture associated with fibrosis.

The muscularis is resistant to distention and because of its density is infiltrated with leukocytes rather late in the course of appendicitis. In the early stages, whether the disease is obstructive or bacterial in origin, there are usually no changes in this layer. In the cases of the obstructive type the muscularis is one of the strongest barriers to perforation. As it becomes thinned by distention and the muscle fibers are separated by accumulation of inflammatory exudate, the continuity of this layer is broken and a microscopic diagnosis of gangrene is made. From this it is seen that a diagnosis of gangrene is not necessarily made from the gross specimen. In cases in which obstruction is not present the inflammatory exudate accumulates, but since there is no distention the layer does not become thinned. This explains in part why perforation is rare in such cases. Obstructed appendixes become distended and thinned, while nonobstructed appendixes are thick walled and soggy with accumulated fluid and cellular exudate. This point is sufficiently characteristic to make the diagnosis of obstruction possible on examination of the section only. In the cases in which an interval preceded operation, as has previously been noted, the muscularis may have appeared normal in the ordinary section but staining with azo-carmin showed marked fibrosis.

The serosa normally contains a rather rich supply of lymph spaces and blood vessels, so that it enters prominently into the changes incident to inflammation. In cases of appendicitis due to obstruction it may show edema and neutrophilic infiltration as early as the submucosa. However, if these changes are seen only in the serosa, a diagnosis of periappendicitis is indicated, as intraperitoneal lesions, particularly those occurring in the pelvic organs of the female, give rise to serositis without involvement of the deeper layers. In cases in which there is no obstruction the serosa shows infiltration with fluid and cells to a degree no less marked than that associated with obstruction. In the series in which operation was delayed the serosa on ordinary stain-

⁹² Thompson, H. G. Lymphoid Tissue of the Alimentary Canal. *Brit. M. J.* 1: 7-11, 1938.

ing showed more marked and constant changes than any other layer. There were always marked increase in vascularity, lymphocytic foci and irregular thickenings of the serosa. These changes represent the end stages of healing of the surface exudate and are closely connected with the process of periappendical formation of adhesions.

The mesoappendix is early the seat of edema and neutrophilic accumulation in obstructive appendicitis, as a result of distention and vascular stasis. Schrumpt⁸⁹ and Noll⁹⁰ also found this to be true. They noted frequent thrombosis of the mesenteric veins in cases of severe involvement, but this has not been observed in this series, although search has been made. In the cases in which there is no obstruction thrombosis of the mesenteric veins is more rarely seen, but has greater significance in that these thrombi are more likely to be infected. This is the most plausible source of abscesses of the liver as a complication of appendicitis. Microscopic sections in cases in which an interval preceded appendectomy showed the same type of fibrosis, vascularity and lymphocytic infiltration in the mesoappendix as in the serosa.

Tabulation of the details of the microscopic pathologic picture in 68 acutely diseased and gangrenous appendices, both of the obstructive and the nonobstructive type gives the following information:

- 1 There is no correlation between the duration of the disease process and the severity of the pathologic change. Apparently the important factor is the severity of the infection or the completeness of the obstruction rather than the number of hours of duration. For example, in 1 case the appendix, obstructed by a fecalith, became gangrenous and ruptured in eight hours, while in another, in which there was also obstruction by a fecalith, only mild inflammation was seen after ninety-six hours.

- 2 Distention of the lumen and flattening of the mucosa by pressure are the two most reliable observations in the obstructed appendix and readily distinguish the obstructive from the bacterial type of the disease as in the latter there never is distention of the lumen or thinning of the wall.

- 3 The mucosa in both the obstructive and the bacterial type may be necrotic and sloughing, but in the obstructed appendix the mucosa is thinned by pressure, while in the infected organ the mucosa is thickened, owing to edema and infiltration.

- 4 The type of cellular exudate is identical in the two varieties of appendical inflammation. The only differential point seems to be the thinning of the wall and dilatation of the lumen in the obstructive type as a result of distention and increased intraluminal pressure.

- 8 *Micrometry of Appendical Wall and Lumen*—Throughout this paper it has been emphasized that distention of the lumen and thinning

of the wall are found distally in the obstructed appendix. In order graphically to emphasize this important point, 75 specimens were selected from normal, acutely diseased and gangrenous appendices in cases of obstructive and nonobstructive appendicitis. These appendices all had been fixed, then split longitudinally and mounted in paraffin before sectioning and staining. Micromasurements were made of the thickness of the wall and the width of the lumen, both distal and proximal, a Filai micrometer calibrated against a hemocytometer chamber being used. These measurements clearly showed the phenomenon of distal distention in the cases in which obstruction was present. The normal appendices showed practically no difference (20 microns) between the thickness of the wall at the base and that near the tip of the appendix. The lumen was shown to be moderately bulbous, being about three times as large toward the tip. In non-obstructed specimens the wall was increased in thickness by about one fourth, and the greatest increase was near the base. This increase in thickness represented infiltration with fluid and leukocytes. There was surprisingly little difference (about 20 microns) between the cases of nonobstructive acute appendicitis and those of the nonobstructive gangrenous type. The lumen showed moderate increase in width, owing to accumulation of pus. In the obstructed specimens the walls showed marked thinning distal to the point of obstruction. In the gangrenous obstructed appendices the thickness of the distal portion of the wall was about one third that of the proximal portion and the diameter of the lumen toward the tip was more than three times as great as that near the base and more than ten times the normal size. These observations are strikingly brought out in figure 8.

9 *Gross Pathologic Picture*—Inspection of the appendix in the earliest stages of inflammation may reveal nothing more than increased turgidity due to edema. Slightly later there are engorgement and tortuosity of the serosal vessels, due to the hyperemia of infection or to the venous stasis of early distention. Up to this time the obstructed and the nonobstructed appendix may have an identical gross appearance except that in the former an obstructive mechanism may be seen or palpated. Later, however, there is a marked difference in the appearance of the two types. The obstructed appendix always becomes more or less tensely distended distal to the point of obstruction, and there is a sharp transition to normal tissue proximal to this point. Distally the thinning wall becomes covered by a shaggy green to yellow fibrinous exudate, which is absent proximal to the obstruction. Proximally only edema and congestion are noted. The omentum or the adjacent loops of small bowel often become adherent to the area of exudate. The gangrenous obstructed appendix is friable, tensely distended and often

surrounded by a cloudy to purulent fluid, which may be sterile. With perforation the distal portion, which is gangrenous, may slough off into the resulting abscess cavity. After the distention is relieved by perforation it may be difficult or impossible to demonstrate an obstructing mechanism. At the operating table such conditions as kinks, adhesive bands and a retrocecal position may be recognized and evaluated as causes of obstruction, but often in their absence it is necessary to "bivalve" the fixed appendix longitudinally in order to determine whether obstruction to the lumen exists. In the nonobstructed specimen

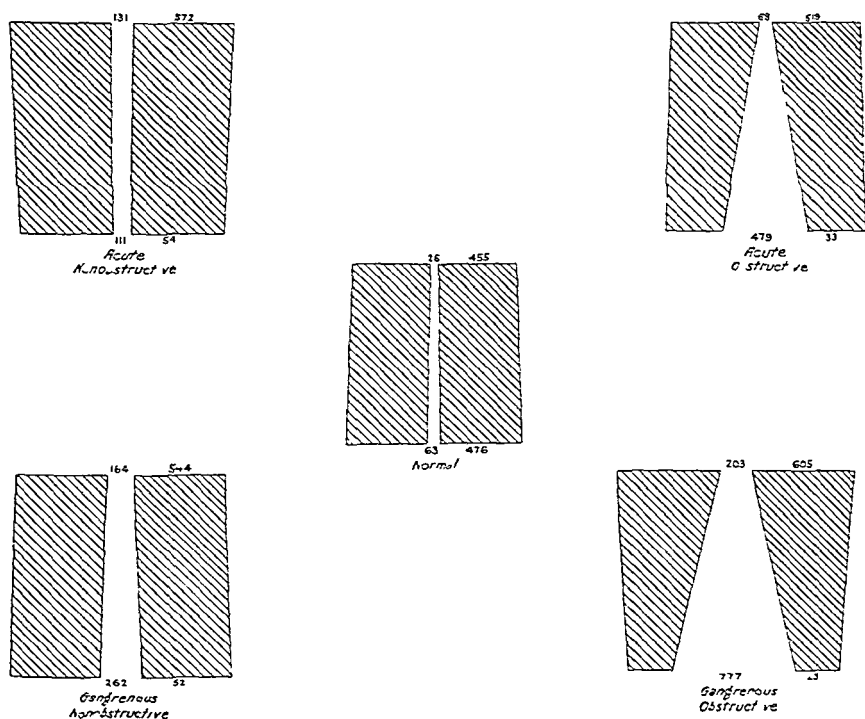


Fig 8—Micrometric data in a series of 75 appendices from the normal, the acutely diseased nonobstructed, the gangrenous nonobstructed, the acutely diseased obstructed and the gangrenous obstructed groups. Measurements were made of the width of the lumen and of the thickness of the wall, both distally and proximally. The average for each group was determined and this chart is a graphic representation of the data drawn to scale. The effect of distention on the wall and on the lumen distal to the point of obstruction is clearly shown. Note that the changes are observed most clearly on longitudinal section. External inspection of the obstructed appendix does not reveal these changes, because the external diameter is fairly constant throughout the length of the organ.

a thick congested soggy wall without distention of the lumen or thinning of the wall usually is seen. Otherwise the appearance is similar to that described for the obstructed specimen.

10 Healing—Healing in appendicitis is accompanied by replacement by fibrous tissue of all structures destroyed by the inflammatory reaction. The changes include (1) obliteration of the lumen if the mucosa is destroyed by ulceration, (2) fibrosis of the submucosa, (3) fibrosis of the musculature, with consequent dysfunction, and (4) thickening, irregularity and increased vascularity of the serosa. The following experiment was undertaken in order to study the microscopic evidences of healing. Forty-three appendixes were chosen, as follows: 7 microscopically normal, 3 acutely diseased, 3 gangrenous, 6 obliterated, 11 "interval" specimens and 13 animal specimens. The sections were stained with hematoxylin and eosin and with azocarmine to show fibrous tissue. The normal appendixes were studied in order to establish a standard for comparison. In the acutely diseased appendixes the serosa

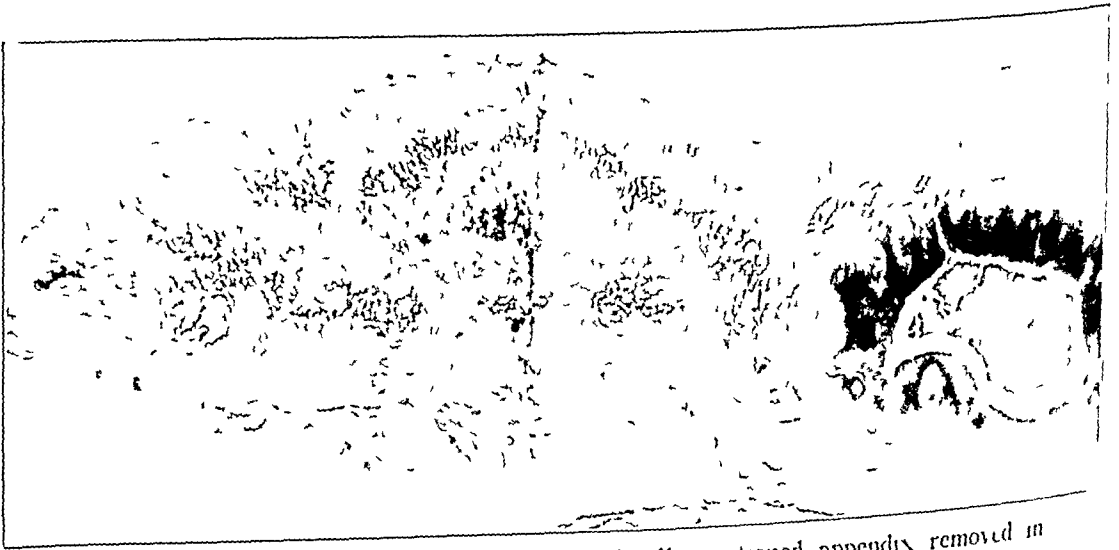


Fig 9—Photomicrograph of a longitudinally sectioned appendix removed in the interval between attacks. This section shows the distal portion of the appendix to be fibrotic and without a lumen or epithelial elements.

was edematous and contained new connective tissue. The muscle fibers were separated by new connective tissue fibrils, and the submucosal vessels were surrounded by collars of new connective tissue and lymphocytes. The gangrenous specimens showed a large amount of fibrinous exudate in all layers, in addition to a dense cellular infiltration throughout the organ. The obliterated appendixes contained a central fibrous core without epithelial elements. In many instances the muscularis was fibrotic, and the muscle fibers were separated into small isolated masses. In some instances there were fibrous tissue collars around the vessels (fig 9). The most striking changes were noted in the "interval" specimens, which were characterized by submucosal fibrosis with perivascular collars, fibrosis of the muscularis and serosal thickening with new connective tissue, lymphocytic foci and abnormal

vascularity. In the animal group specimens showing acute changes, gangrene and various stages of healing were chosen and studied with the azocarmine stain. The results paralleled in all particulars the observations on the clinical material.

11 *Organic Residual Changes*—The actual organic residual changes of appendicitis include obliteration, stenosis, fibrous septums dividing the lumen into locules, mucocele formation, diverticula and granulomatous thickening of the wall. Letulle⁹³ mentioned all of these changes as being due to previous inflammation. The controversy as to whether obliteration represents healed inflammation or a normal physiologic process of age will not be discussed in this paper.

Many bizarre observations are reported in the literature. For example, Berger and Simon⁹⁴ reported a case in which the appendix had been amputated spontaneously and was lying free in an abscess cavity. Piraja⁹⁵ reported a case in which the inflamed tip had eroded through the posterior aspect of the cecum, and at subsequent operation the appendix was observed to have two cecal orifices.

Peterson⁹⁶ stated that 172 cases of mucocele of the appendix have been reported. These reports have usually dealt with large cysts, and no doubt many hundreds of instances of smaller ones have not been reported. If obliteration of the lumen occurs first at the base, rather than at the tip, a closed cavity is formed. The organisms gradually die out, and the sterile cavity slowly increases in size, owing to accumulation of mucus. This slow increase in size does not embarrass circulation, so that no acute inflammatory process develops. Josa⁹⁷ observed *B. coli* in a mucocele but expressed the belief that the cavity gradually tended to sterilize itself. Horsley and Warthen⁹⁸ concurred in these views. Collins⁹⁹ observed at autopsy an incidence of obliteration of 39 per cent in a series of 1,054 appendixes. In 3 per cent the obliteration

93 Letulle, M. Les surprises de l'appendicite chronique. *Presse med* **35** 1521-1523, 1927.

94 Berger, J., and Simon, R. Evolution vers la resorption d'un appendice ampute spontanement et flottant dans un abces, *Bull et mem Soc nat de chir* **60** 1026-1029, 1934.

95 Piraja, O. Appendice cecal com dupla implantacao, *Ann paulist de med e cir* **27** 233-239, 1934.

96 Peterson, R. F. Mucocele of the Appendix. Report of Two Cases, *Northwest Med* **23** 328-330, 1934.

97 Josa, L. Leber einen seltenen Fall von Appendicitis phlegmonosa im obliterierten Wurmfortsatz. *Zentralbl f Chir* **62** 259-262, 1935.

98 Horsley, J. S., and Warthen, H. J. Jr. Pathogenesis and Symptoms of Chronic Obliterative Appendicitis. *Ann Surg* **96** 515-529, 1932.

99 Collins, D. C. Mechanism and Significance of Obliteration of the Lumen of the Vermiform Appendix. *Ann Surg* **104** 199-211, 1936.

began at some point other than the tip. That residual organic changes tend to follow appendicitis is shown by the following tabulation:

	Acute Appendicitis		Gangrenous Appendicitis		Appendectomy After Interval		Gynecologic Group	
	Cases	%	Cases	%	Cases	%	Cases	%
Residual changes	5	5	8	10	50	34	7	12

The number of cases in which the various residual changes were observed were as follows:

	Acute Appendicitis	Gangrenous Appendicitis	Appendectomy After Interval
Obliteration	2	0	25
Stricture	4	0	13
Fibrous septums	0	7	0
Adhesive bands	1	5	0
Kink	1	5	0
Mucocele	0	0	2
Diverticulum	0	0	2

It is of interest to note that in the cases of acute and gangrenous appendicitis due to obstruction there was an incidence of organic residual changes of 28 per cent as compared with the absence of such changes in the cases in which obstruction was not present (fig 10).

In these studies many interesting observations have been made in the microscopic sections. In 5 of the cases of appendectomy after an interval the area of previous perforation could be visualized clearly. The accompanying photomicrograph is illustrative (fig 11). In 2 cases a lymphoid follicle had acquired a pedicle and had become polypoid. In 1 case of the acute form there was a definite abscess in the wall of the appendix, and in 1 case a fecalith was being pushed through a perforation in the appendix. In 2 other cases there were high polypoid mucosal rugations.

In every case in this series the inflammatory process was most severe toward the tip of the appendix. In no case was there basal gangrene with a noninflamed tip. Orthner,¹⁰⁰ on the other hand, reported an incidence of basal gangrene of 2 per cent in otherwise normal appendixes. He stated that this condition is usually symptomless and that perforation takes place before the diagnosis can be established. Handley¹⁰¹ described a similar process in which perforation occurs into the fatty layers between the leaves of the mesentery. This leads to spreading retroperitoneal cellulitis rather than to peritonitis and is not accompanied by rigidity or other signs of peritonitis. This phenomenon is rare in man, but is seen frequently in the dog. It is most often due to perforation through the bowel into the mesentery by a foreign body in the lumen.

¹⁰⁰ Orthner, F. Die basale Gangren des Wurmfortsatzes, *Schweiz med Wchnschr* **65** 92-93, 1935.

¹⁰¹ Handley, W. S. Basal or Cellulitic Appendicitis, *Clin J* **64** 1-3, 1925.



Fig 10—Appendix showing the fibrous septums resulting from previous attacks of appendicitis and partially dividing the lumen into three distinct compartments, two of which contain fecaliths. The small fecalith is not shown in the original position of impaction, but it will be noted that the lumen proximally is normal in caliber and the walls are of normal thickness.

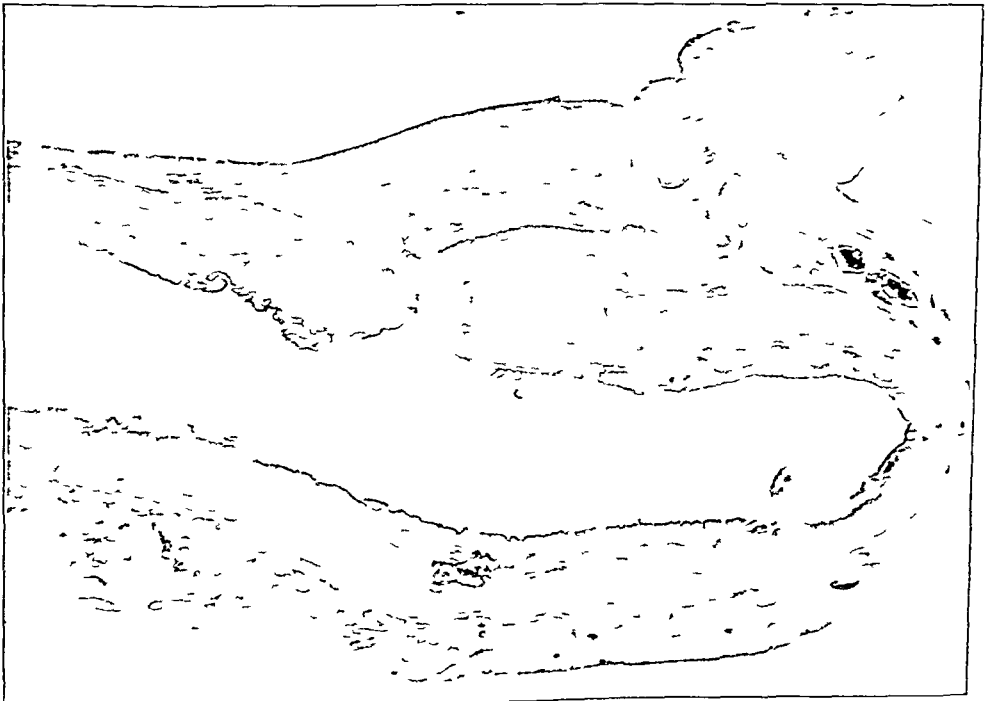


Fig 11—Appendix removed six weeks after the original peritonectomy. It can be seen that the defect in the wall has not healed but has been covered by exuberant granulation tissue and infected edematous serosa. A slight increase in intraluminal pressure would readily initiate a second peritonectomy with peritoneal soiling.

(a) Colic Group In the Minneapolis General Hospital series there were 5 cases which have been considered in a separate group. In these cases (the patients were all girls, with an average age of 19 years) the average duration of appendicitis, of mild type, was one hundred and twenty hours. Nausea and constant pain were present in 81 per cent, with vomiting and rigidity in half that number. All the patients had pain in the right lower quadrant, and 60 per cent had rebound tenderness. Sixty per cent gave a history of similar previous attacks. The average temperature was 99.8 F, the average pulse rate was 86 and the average white blood cell count was 11,825, with 73 per cent neutrophils. These 5 girls were operated on, and in each case the appendix was microscopically normal, without any signs of present or past inflammation. However, there was an obstructing fecalith in every case, and in 80 per cent a distally dilated lumen gave evidence of some increased intraluminal pressure. In 40 per cent there were bacteria in the tissues. The condition in these cases was the so-called colic type of appendicitis, which is to be explained on one of the following bases: 1. It may represent simply a mild form of closed loop with incomplete obstruction, so that the more severe late effects are absent. 2. It may be caused by purely mechanical factors, the musculature contracting in an effort to expel the fecalith and producing the same type of pain as that seen in intestinal obstruction in which the intermittent peristalsis causes cramp-like pains. All of the patients were relieved by appendectomy. This is illustrative of the fact that removal of a microscopically normal appendix may cure the patient. Pathologists as yet have no way of classifying such dysfunction and are apt to criticize a surgeon for removing a so-called normal appendix. Mayo¹⁰² also has shown that removal of the appendix in 100 cases of obscure pain in the right lower quadrant gave relief in 70 per cent.

12 *Periappendicitis*—Periappendicitis, as described by Gordon,¹⁰³ is an inflammatory change limited to the serosa and due to pelvic inflammatory disease or to some other peritoneal infection. In 62 appendixes removed incidental to some gynecologic procedure¹⁰⁴ there was an incidence of periappendicitis of 16 per cent. This condition is symptomless because there is no distention, and often is not diagnosed.

¹⁰² Mayo, C. W. Exploration of Abdomen and Appendectomy for Atypical Symptoms. Results Five Years After Operation in One Hundred Cases, *West J Surg* **42** 189-190, 1934.

¹⁰³ Gordon, H. Periappendicitis Without Appendicitis. Study Based on 26,051 Appendixes, *Arch Path* **19** 185-202 (Feb.) 1935.

¹⁰⁴ Shute, E. Invagination of Appendical Mucosa Producing Symptom Resembling Appendicitis, *Arch Surg* **27** 75-82 (July) 1933.

on examination of the gross specimen. In 11 per cent of the specimens there were bacteria in the superficial tissue layers, and in 10 per cent over the surface of the serosa. In 25 per cent of cases there were fecaliths in the lumen but in only 1 per cent were there evidences of actual obstruction. This emphasizes the harmlessness of fecaliths in the absence of obstruction to the lumen. This was brought out most clearly in an autopsy specimen in which there was a large fecalith in the tip of the appendix. There was no remaining mucosa around this fecalith, which was completely walled off by fibrous tissue. There



Fig 12—Autopsy specimen. The illustration shows why some fecaliths may be present for years without initiating acute appendicitis. The fecalith has destroyed the surrounding mucosa by pressure and now is actually walled off and lies distal to the termination of the lumen. Since there is no obstruction and the fecalith is not surrounded by a secreting mucosa, no distention develops and there is no inflammation, although there are bacteria distally in the tissues, as seen in a Gram tissue stain.

could be no harmful effects because in the absence of a secreting mucosa distention could not develop. The Gram stain showed organisms in the fecalith and around its edges with some in the tissues (fig 12).

Periappendicitis was seen in 5 autopsy specimens. One was obtained in a case of dysentery with perforation of ulcers of the colon and

peritonitis The appendix showed acute serositis with mixed organisms in the serosa Another specimen was from a patient who died of perforation of a duodenal ulcer A third was from a patient with post-operative peritonitis, and the other 2 were from patients with primary pneumococcic peritonitis These last specimens showed gram-positive diplococci in the serosa

APPENDICOLITHS

1 *Incidence*—In this series the incidence of fecaliths for the entire group of cases of acute appendicitis was 67 per cent, and in 16 per cent of these cases there were multiple stones In no case was

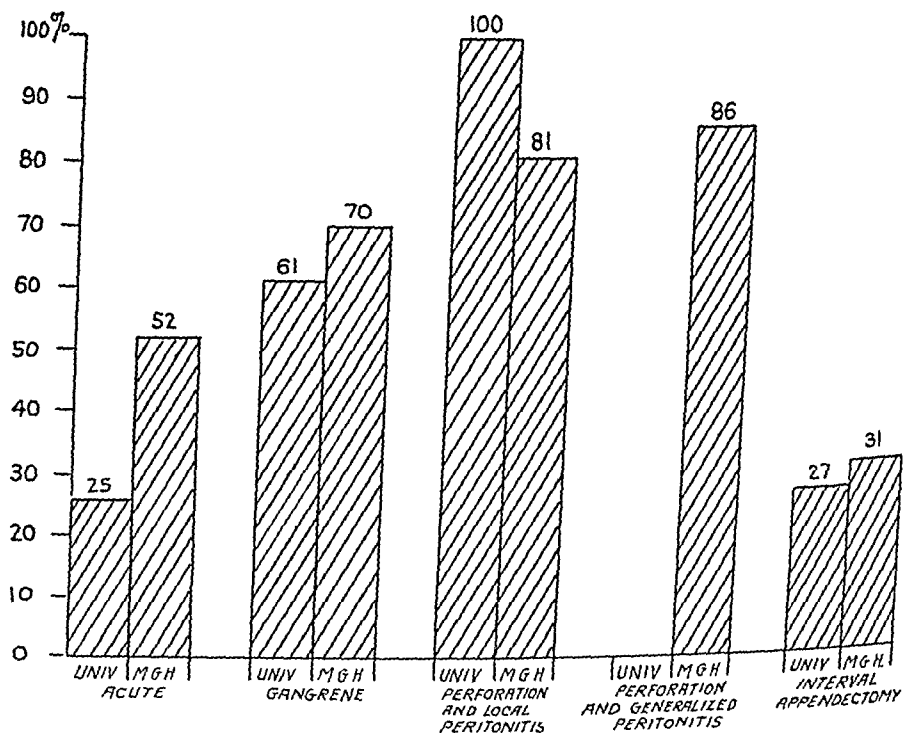


Fig. 13—Incidence of fecaliths in the various types of appendicitis in this series

inspissated fecal material (fig 13) classed as a stone The incidence of appendicoliths was distributed among the groups as follows

	Acute Appendicitis		Gangrene		Localized Peritonitis		Generalized Peritonitis		Colic		Appendectomy After Interval		Gynecologic Group
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	
Minneapolis General Hospital	25	52	14	70	10	81	19	86	5	100	5	1	1
University Hospitals	11	25	35	61	4	100					27	12	1
Average		38		65		90		86		100		29	2

2 *Microscopic, Chemical and Roentgenographic Data*—Roentgenograms of these appendicoliths were taken routinely and all showed laminations due to successive concentric deposits (fig 14) Many of the stones were sectioned and examined microscopically In one case there was a large amount of cellulose material (fig 15) 11

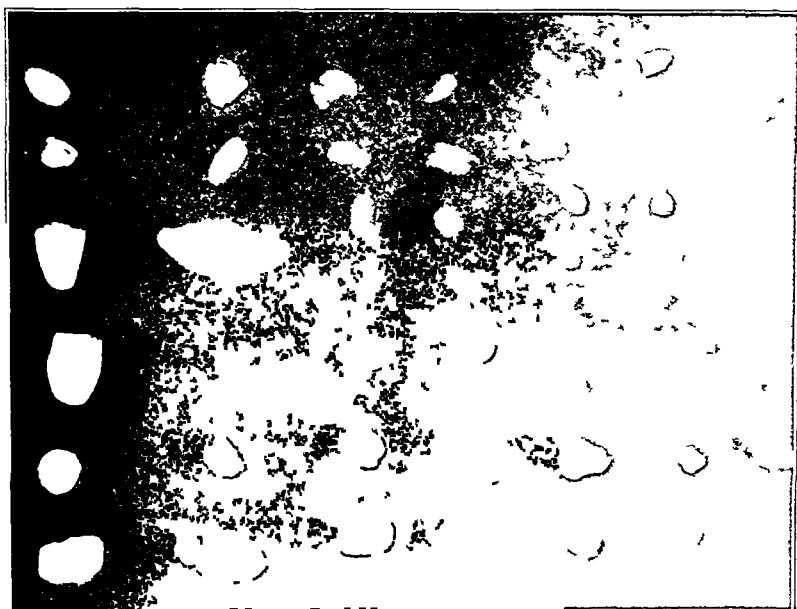


Fig 14—Roentgenogram of a group of fecaliths, demonstrating their laminated structure. This indicates that they probably form in situ but does not give any suggestion as to their age, as the rapidity with which laminas are laid down is not known.

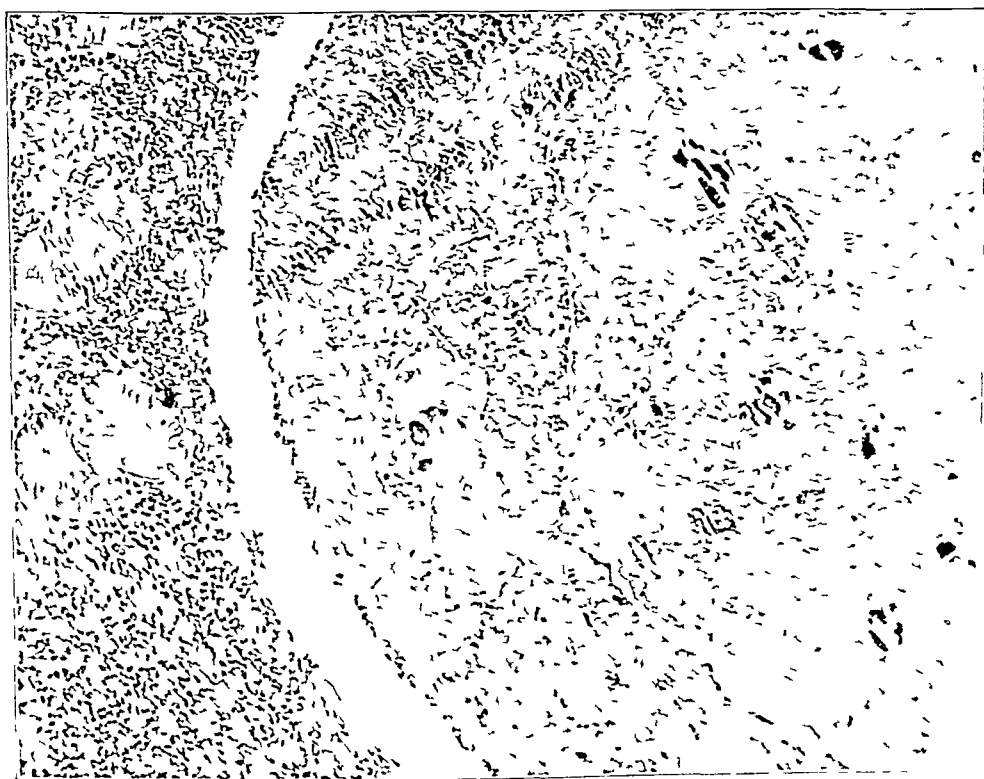


Fig 15—Photomicrograph showing the laminated character of a fecalith. The densely stained areas are calcium. Masses of cellulose and amorphous material are seen to make up the greater portion of the stone.

Gram stain revealed dense masses of bacteria throughout the concretion. There usually was a central nidus, which was often a mass of cellulose. Parasites were seen in a number of fecaliths, but this has been discussed previously. In 4 cases blueberry seeds (*Vaccinium pennsylvanicum*) formed the nidus and were identified on microscopic section (fig 16). On questioning, 1 of the patients was positive that she had not eaten blueberries for over two years. This probably was inaccurate, but at least it indicates a long period of stasis in the appendix. In 3 cases small brown shiny faceted stones resembling gallstones, were observed



Fig 16—Photomicrograph of a blueberry seed within a fecalith, illustrating how such foreign bodies may form a nidus about which a fecalith is deposited in successive laminae.

in the appendix, and in 1 case these stones seemed to be identical with those removed from the gallbladder at the same time.

An attempt was made to determine the nature of the pigment in appendicoliths. Chemical tests for bilirubin, biliverdin, urobilin and urobilinogen on several occasions all gave negative results. In view of the high calcium content of the stones, as will be shown later, it is probable that the pigment is a calcium salt of one of the reduced forms of bile pigment, probably kopronegrin.

A group of fecaliths was analyzed for organic and inorganic material. A group of scybalous masses of normal stool was similarly analyzed for comparison. Table 5 shows the comparative results.

There are two types of appendicoliths: those which are hard, white and odorless and those which are softer and brown and have a fecal odor. Both types are laminated and radiopaque and usually have a central nidus composed of cellulose, parasites or foreign bodies, such as seeds, bristles, pins or enamel from kitchenware.

It is impossible to state the normal incidence of fecaliths, but there are a number of references to their frequency in inflamed appendices. Fitz³ reported an incidence of 47 per cent of fecaliths and 12 per cent of foreign bodies in a series of 152 cases of appendicitis and stated that in about 60 per cent of all cases perforation is caused by fecaliths.

TABLE 5—*Chemical Analysis of Fecaliths**

	Fecaliths %			Stool Nugget %		
	Original	Dried	Ash	Original	Dried	Ash
Calcium	8.04	12.03	33.04	4.10	4.30	29.35
Phosphorus	4.59	7.07	18.07	2.01	2.15	14.35
Magnesium	0.80	1.29	3.25	0.8	0.86	5.74
Sulfur	0.0	0.0	0.0	0.74	0.89	5.50
Chlorine	0.0	0.0	0.0	0.12	0.125	0.55
Volatile material at 110 C			37.82			6.91
Ash Original			24.32			13.95
Dried			29.12			14.05
Free lipoids			13.0			
Fatty acid			3.35			
Free cholesterol			6.65			

* The results of this analysis indicate that the fecalith is not merely an indurated fecal mass but is a definite concretion.

or foreign bodies. He cited Matterstock as finding 53 per cent of fecaliths and 12 per cent of foreign bodies in a series of 169 cases of fatal perforative appendicitis. Aschoff¹³ in 1905, said that in most cases appendicitis occurs in the stone-free appendix but this observation does not hold true for the series of most investigators. He stated that fecaliths are harmless unless infected but most observers find it difficult to conceive of a sterile fecalith. In his monograph, published in 1908 Aschoff¹⁴ gave the following data:

	22 Cases of Normal Appendicitis	177 Cases of Appendectomy After Interval	122 Cases of Acute Appendicitis
Fecal Fecaliths	67% 67%	62% 12%	10% 27%

These figures are extremely low as compared with those of other observers although Burgess²¹ found that only 21 per cent of 500

appendixes contained fecaliths. He observed fruit seeds in several and pinworms in many. Williams and Boggon⁵² reported that 39 per cent of appendixes with an acute condition contained fecaliths.

The general impression is that appendicoliths form in situ, successive laminae being deposited about some extraneous nidus. This impression is based on the fact that the concretions frequently reach the size of walnuts (Wells¹⁰), being much larger than the lumen of the appendix,

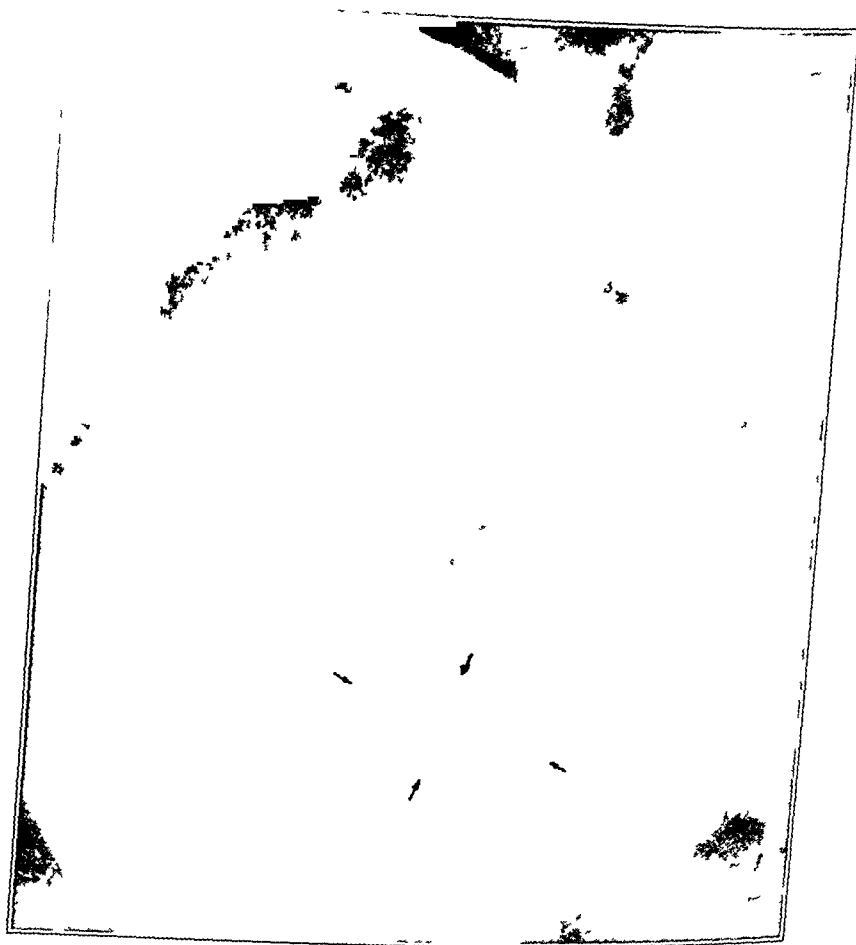


Fig 17—Scout roentgenogram of the abdomen in the case of a 19 year old youth who had a history of nausea and vomiting of forty-eight hours' duration, accompanied by tenderness, rebound tenderness and rigidity in the right lower quadrant of the abdomen. There had been no previous attacks. The temperature was 101 F, the pulse rate 92 and the leukocyte count 11,500 per cubic millimeter, with 82 per cent neutrophils. A mass 5 cm long was palpable in the right lower quadrant. The plate shows one large and one small fecalith, easily recognizable by the concentric lamination. A tensely distended, gangrenous, obstructed appendix was removed, and the fecaliths were recovered. The palpable mass might be mistaken for regional enteritis, but the scout roentgenogram clinches the diagnosis of appendicitis, as ureteral stones are not laminated in this way.

105 Wells, C. A. Appendix Concretions Opaque to X-Rays, *Brit. M. J.* 2 1041-1042, 1930.

and that all fecaliths are made up of concentric laminations about some central mass (figs 17 and 18) of foreign material (Volz¹)

It is a common observation that sections of fecaliths show large quantities of cellulose. Mayer and Wells¹⁰⁶ demonstrated sclerous vegetable material, granules of silicates and occasional parasitic ova. These authors analyzed several groups of fecaliths, and they found one half of the material by weight to be soluble in fat solvents. This was chiefly soap, although there was some koprosterol and a little cholesterol. About one fourth of the total weight was composed of inorganic salts, chiefly calcium phosphate, and about one fifth of the total weight was

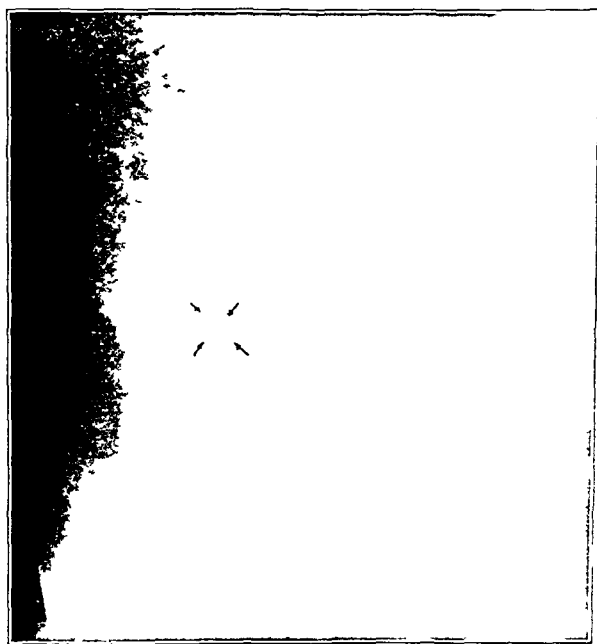


Fig 18—Roentgenogram taken after a barium enema in the case of a 56 year old man who gave a history of repeated abscesses in the lower right quadrant of the abdomen following rupture of the appendix. A large, laminated fecalith is seen below the cecum and in the region of the abscess, which deforms the base of the cecum.

organic residue, mostly vegetable fibers from the cecum. It is to be noted that bile pigments and bile acids usually are absent.

3 Foreign Bodies—Several interesting foreign bodies were observed in the appendices studied. In 1 case the appendiceal lumen contained a small spicule of bone which was piercing the wall. The lumen

106 Mayer M E and Wells H G. Composition of Appendiceal Concretions. Arch Surg 3: 439-444 (Sept.) 1921.

contained pus. In another case the lumen contained a piece of keratinized material resembling finger nail. In a third instance a tooth-brush bristle was seen in the lumen.

CLINICAL MANIFESTATIONS

1 *Symptoms*—(a) *Average Hours of Duration* As would be anticipated the average duration of symptoms, in terms of hours, is correlated with the severity of the disease process. In this series appendicitis due to obstruction tended to have a shorter course (twenty-three hours) than the nonobstructive condition (thirty-two hours). The following data show the average number of hours of duration for the various types.

	Acute Appendicitis	Gangrene	Localized Peritonitis	Generalized Peritonitis
Minneapolis General Hospital	70 hr	36 hr	79 hr	66 hr
University Hospitals	43 hr	31 hr	24 hr	
Average	51 hr	33 hr	51 hr	76 hr

It will be noted that in the cases of acute appendicitis the duration was longer than in the cases of gangrene. This is because acute appendicitis is less severe than the gangrenous type, and the patient postpones seeking medical aid.

(b) *Pain* The pain of acute appendicitis is of two types, constant and colicky. In the average for the entire series, the colicky type was found in 31 per cent of cases and the constant pain in 56 per cent. This difference is more striking when the cases are divided according to the presence or absence of obstruction. In cases of the nonobstructive type colicky pain was found in 32 per cent and constant pain in 33 per cent, whereas in cases of the obstructive type colicky pain was present in only 12 per cent and constant pain in 74 per cent.

(c) *Nausea* This symptom is much more frequent in acute appendicitis than vomiting, the former being seen in 90 per cent of cases and the latter in 68 per cent. In cases of the obstructive type, nausea was found in 81 per cent and vomiting in 64 per cent. In cases of the nonobstructive condition nausea was observed in 88 per cent and vomiting in 58 per cent.

(d) *Constipation* This condition was present in 13 per cent of cases in this series, and there was no apparent correlation between this factor and obstruction.

2 *Physical Signs*—(a) *Tenderness* The most frequent finding in acute appendicitis is tenderness, which was elicited in 98.5 per cent of all cases. There is no significant difference in the obstructive and the nonobstructive type in this regard.

(b) *Rebound Tenderness* The next most frequent physical sign is rebound tenderness, which was present in 87.5 per cent of all cases.

in this series. In this respect there was an appreciable difference between the obstructive and the nonobstructive type, the incidence in the former being 75 per cent and that in the latter 59 per cent.

(c) *Rigidity* Rigidity was elicited in 85 per cent of cases. In the cases of obstructive appendicitis rigidity was demonstrated in 92 per cent, and in those of the nonobstructive type, in 68 per cent.

(d) *Murphy's Sign* The Murphy sign is pain in the right lower abdominal quadrant caused by pressure of the hand on the left lower quadrant, and it depends on pressure of abdominal organs or colonic contents on the inflamed appendix. This sign was positive in 29 per cent of cases.

(e) *Head's Area of Hyperesthesia* Head's area of cutaneous hyperesthesia in the right lower quadrant was present in 22 per cent of cases.

(f) *Mass* Palpation revealed an abdominal mass in only 6 per cent of cases, and the incidence was correlated with the severity and stage of the disease process, it being five times as great in cases of the perforated as in those of the nonperforated type. In only 1 case was the appendix palpable through the abdominal wall, and in this case the organ was obstructed and extremely distended.

(g) *Tenderness on Rectal Examination* Rectal examination revealed tenderness high on the right side in 65 per cent of cases.

3 *Laboratory Data*—(a) *Temperature* The average temperature for the entire series of cases of acute appendicitis was 100.2 F, the temperature following the severity of the process, as follows:

Acute Appendicitis	Gangrene	Localized Peritonitis	Generalized Peritonitis
99.6 F	100.2 F	100.8 F	101.2 F

There was no noticeable difference between the obstructive and the nonobstructive condition as far as fever was concerned. The average temperature in the series of delayed appendectomy was 99 F. In each type of the disease the average temperature was about 1 degree Fahrenheit higher for the pediatric age group than for the adults.

(b) *Pulse Rate* The average pulse rate in the entire series was 96, there being a correlation between the rate and the severity of the disease. The average pulse rate in cases of obstructive appendicitis was 82 as compared with a rate of 108 in the cases of nonobstructive appendicitis. This seems to be a differential diagnostic point but unfortunately it is apparent only in the average for a group of cases. The pulse rates were as follows:

	Acute Appendicitis	Gangrene	Localized Peritonitis	Generalized Peritonitis	Appendectomy After Interval
Minneapolis General Hospital	94	100	92	100	88
University Hospitals	92	96	92	96	88
Average	93	98	92	98	88

In each type of the disease the pulse rate averaged 10 points higher for the pediatric group than for the adult

(c) **Leukocyte Counts** An increased leukocyte count does not necessarily indicate infection (Downey,¹⁰⁷ Pepper and Farley¹⁰⁸), as the average preoperative count in a series of 10 cases of noninfected strangulated hernia was 12,500 per cubic millimeter. The leukocyte count, particularly the Schilling count, in cases of appendicitis is of importance in several respects. Warnock¹⁰⁹ found that the Schilling count reduced the incidence of discrepancies between the preoperative diagnosis and the microscopic observations. Hellwig¹¹⁰ found the total leukocyte count to be misleading because in cases of fatal appendicitis there frequently was not a high count even when peritonitis was present. He therefore opposed basing treatment on the white cell count. It is said that Ochsner always ordered a white cell count but never looked at the result until after the operation. Carlson and Wilder¹¹¹ found the Schilling count to be superior to the total leukocyte count and of more value than the temperature or the pulse rate in determining the severity of the disease process. A low leukocyte count or a shift to the left may indicate a poor prognosis. The leukocyte count in this series gave the following information:

	Appendectomy After Interval	Acute Appendicitis	Gangrene	Localized Peritonitis	Generalized Peritonitis
Average count	9,420	15,000	18,170	18,000	18,000
Under 10,000	100%	5%	5%	4%	9%
10,000 to 15,000	0	59%	24%	25%	28%
Over 15,000	0	36%	71%	71%	63%
Neutrophils					
Average number	63	79	84	86	86
Under 70	100%	15%	8%	0	5%
71 to 80	0	27%	15%	0	15%
81 to 90	0	46%	63%	79%	67%
Over 90	0	12%	17%	21%	30%

In the cases of obstructive appendicitis the total average white cell count was 16,000 per cubic millimeter as compared with 13,800 in the cases of nonobstructive appendicitis. The neutrophil counts in the two groups agreed fairly closely. In the pediatric age group the average white cell count was higher by about 2,000 cells than that in the adult group in each type of the disease.

107 Downey, H. Personal communication to the author.

108 Pepper, O. H. P., and Farley, D. L. *Practical Hematological Diagnosis*. Philadelphia, W. B. Saunders Company, 1933.

109 Warnock, F. B. Leucocyte Count and Histopathology in Acute Appendicitis, *Am J Surg* **21** 47-55, 1933.

110 Hellwig, C. A. Leucocyte Count in Acute Appendicitis, *J Kansas Med Soc* **29** 330-334, 1928.

111 Carlson, H. A., and Wilder, L. Schilling Hemogram in Appendicitis, *Arch Surg* **30** 325-335 (Feb) 1935.

(d) Urinalysis Microscopic examination of the centrifuged specimens of urine showed red blood cells in 7 per cent of cases and leukocytes in 14 per cent. There was no significant distribution among the various types of lesions, nor was there a correlation with the presence of obstruction to the lumen of the appendix.

Wilkie¹¹² stated the opinion that the obstructive and the non-obstructive type of appendicitis can be differentiated clinically. He stated that obstructive appendicitis tends to cause little elevation of the pulse rate and temperature. In this investigation certain distinguishing points have been noted, but these are evident only in consideration of the group as a whole. It was not possible to diagnose obstruction of the appendix with any degree of accuracy, although the frequency of the condition makes such a diagnosis more often right than wrong.

CONCLUSIONS

1 It has been shown that in a series of 372 cases of appendicitis there was a definite organic obstruction to the lumen in 80 per cent. The obstructing mechanism was an impacted fecalith in 67 per cent of these cases. When neuromuscular and other factors are considered in the future the incidence of obstruction may be found to be much higher.

2 A study of the seasonal incidence of appendicitis over a period of eight years has shown an even distribution throughout the year. This is in accord with the idea that appendicitis is more often an obstructive phenomenon than a specific bacterial disease.

3 An inverse correlation between the history of previous attacks and the severity of the disease has been demonstrated. This is because the mild attacks tend to regress spontaneously, whereas the more severe forms usually require early operation. It is also important to note that the incidence of obstruction is much greater in cases of severe involvement.

4 It has been shown that normal excised appendices respond to faradic stimulation for an average of three and one-half hours, whereas inflamed appendices have such damaged musculature that an average response of only twenty-six minutes is seen. This is important in understanding why fibrosis and dysfunction may follow healing of the appendix.

5 It has been shown in a clinical experiment that distention of the appendiceal lumen is capable of causing a train of symptoms similar to that seen in acute appendicitis.

¹¹² Wilkie D. P. D. Observations on Mortality in Acute Appendicitis. *Br. M. J.* 1:253-255, 1931. footnote 19.

6 It has been demonstrated that culture methods and the Gram stain of tissue sections are about equally effective in determining the incidence of bacteria in the appendix. Culture methods, of course, are required for identification of the bacteria. The bacteriologic investigations presented here throw no light on the etiologic factors in appendicitis and simply indicate that a mixed flora is present.

7 The healing of appendicitis has been studied by means of special stains and the process has been observed to be one of fibrosis. It is thought possible to diagnose previous attacks by examination of microscopic sections.

8 Comparison of the histologic appearance of obstructed and that of nonobstructed appendices has shown that the type of inflammatory process is identical in the two groups. The sole difference lies in the fact that the obstructed organs show marked thinning of the wall and distention of the lumen distal to the obstruction, whereas the wall and lumen are nearly uniform in size throughout the length of the nonobstructed appendix. These striking differences have been shown graphically by micrometry.

9 Definite organic residual signs of appendicitis have been observed in 16 per cent of cases in the entire series, that they predispose to further attacks is shown by the fact that in the cases of obstructive appendicitis there was an incidence of organic residual signs of 28 per cent as compared with the absence of such changes in the cases of nonobstructive appendicitis.

10 Chemical, roentgen and microscopic studies of appendicoliths have been made and the results recorded. It is thought that these concretions form in situ. The incidence of parasites and foreign bodies in the lumen also is mentioned.

11 From a complete analysis of the clinical cases, it does not seem possible to diagnose obstructive appendicitis with any degree of surety. The obstructive condition tends to cause more constant pain, rebound tenderness and rigidity with a lower pulse rate, but these differences are slight and are apparent only in the average for the entire group.

PRIMARY ISOLATED LYMPHOGRANULOMATOSIS (HODGKIN'S DISEASE) OF THE STOMACH

REPORT OF A CASE

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Isolated gastric Hodgkin's disease is rare Steindl,¹ in 1924, reported the first case in the literature Singer,² in 1931, collected 6 cases from the literature, added 1 case of his own and made a complete resume of the subject It was he who emphasized that Hodgkin's disease isolated in the stomach is an operable lesion and that with removal of the diseased tissue the prognosis is good This idea was at variance with the accepted therapy of Hodgkin's disease, for since the time of Billroth the condition had been placed in the category of medical diseases

REPORT OF CASE

History—N S, a white woman aged 63, was admitted to the John Gaston Hospital on June 15, 1937, complaining of "indigestion" of six months' duration The indigestion was characterized by epigastric fullness and burning pain which had no relation to food intake Loss of weight and strength had been rapid since the onset, and the digestive disturbances had been progressively more pronounced One month prior to her admission to the hospital the patient first noticed constipation and tarry stools At about the same time nausea and irregular vomiting began The vomitus contained food, and occasionally "coffee grounds" were present

In May 1937, six weeks prior to her admission to the John Gaston Hospital, the patient had been in another hospital where a diagnosis of carcinoma of the stomach was made Operation was advised at that time, but the patient refused to permit it and left the hospital After two weeks, in which the vomiting had become more regular and disturbing she came to the John Gaston Hospital desiring operation

Except for the facts just detailed the past history was irrelevant

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The illustrations for this paper were prepared by Dr J L Scianni medical illustrator of the Department of Pathology

1 Steindl, H Ueber einen Fall von Lymphogranulomatose des Magens Arch f klin Chir **130** 110 (April) 1924

2 Singer, H A Primary Isolated Lymphogranulomatosis of the Stomach Arch Surg **22** 1001 (June) 1931

Physical Examination—The temperature was 98 F, the pulse rate, 80, and the blood pressure, 178 systolic and 95 diastolic. The patient was well developed but showed general signs of recent loss of weight.

The only remarkable physical findings were in the abdomen, where there was a firm, tender, freely movable mass about 7 cm in diameter occupying the mid

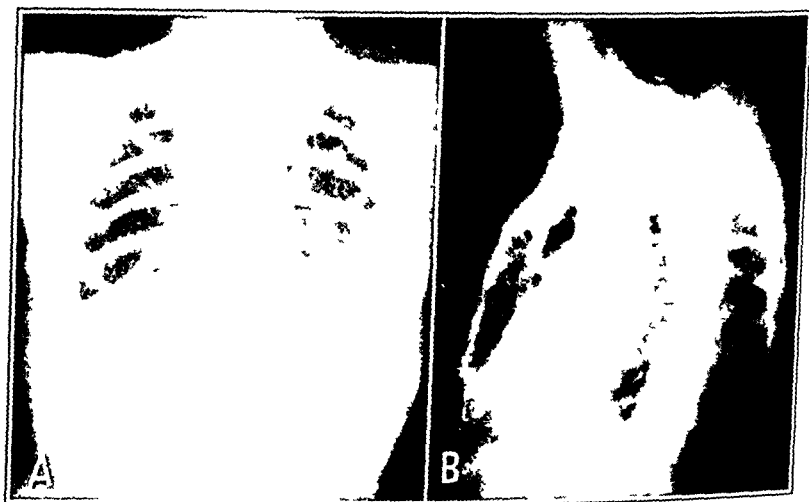


Fig 1—A, anteroposterior film of the chest, showing no mediastinal enlargement. B, lateral film of the chest, showing no mediastinal enlargement.



Fig 2—Film taken after the ingestion of barium sulfate, showing a large prepyloric deformity which was interpreted as a malignant ulcer.

epigastrium. The liver and spleen were not palpable. No abdominal masses were palpable.

Laboratory Findings—The Wassermann and Kahn reactions were negative. The red blood cell count was 3,750,000 per cubic millimeter. The value for hemoglobin was 13 Gm. The white cell count was 11,750 per cubic millimeter, with lymphocytes 26 per cent, neutrophils 71 per cent, basophils 1 per cent and eosinophils 2 per cent.



FIG 3—Operative specimen (three fourths of the stomach) It is opened along the lesser curvature. Note the large ulcer crater with its rolled, and in places inverted edges.



FIG 4—Photomicrograph ($\times 70$) showing the normal gastric glands and the submucosal lymphocytic infiltration extending well into the muscle layer and the areas of scar tissue.

2 per cent. The urine was normal. The stools and vomitus contained blood. Because of the blood in the vomitus, analysis of the gastric contents was not done.

Roentgen Examination—Roentgenograms of the chest (fig 1) were normal. There was no mediastinal enlargement. After administration of barium sulfate



Fig 5—Photomicrograph ($\times 750$) showing the infiltrating lymphocytes and plasma cells. One giant cell of the Dorothy Reed type is seen also in this field.

a large prepyloric defect was seen (fig 2). Gastric retention of the substance at six hours was 50 per cent.

The roentgenologist made a diagnosis of carcinoma of the stomach, and I agreed with him.

After four days of preparation with intravenous administration of dextrose and gastric lavage, laparotomy was performed with the patient under ether anesthesia.

There was a mass about 6 cm in diameter occupying the prepyloric region of the stomach. The mass had the firm consistency of carcinoma and was freely movable. There was no enlargement of the neighboring lymph nodes. The liver and spleen and the mesenteric and retroperitoneal glands did not show any macroscopic or palpable pathologic condition. Believing that the growth was carcinoma of the stomach, I did a wide resection, removing three fourths of the stomach and 5 cm of the duodenum. Continuity of the intestinal canal was effected by a posterior, end to side gastrojejunostomy.

The patient died on the fourth postoperative day, of bronchopneumonia. Post-mortem examination was not permitted.

Pathologic Examination—Macroscopic. The specimen consisted of a portion of the stomach and the adjoining part of the duodenum. When the stomach was opened there was seen an irregularly oval ulceration measuring 9.5 by 5.5 cm in its greatest diameters. It was immediately prepyloric (fig. 3). The edges of the ulcer were rolled and in certain areas were inverted. The wall of the crater sloped irregularly to a depth of 1.5 cm. The base of the ulcerated area was firm, granular and mottled gray to yellow. The wall of the stomach varied in thickness up to 1.5 cm. The muscular layer was thickened. A few omental tags were adherent to the serosal surface, but there was no evidence of perforation.

Microscopic. The mucosa showed moderate infiltration with lymphocytes and plasma cells. There was an occasional eosinophil. The glands were essentially normal. There was an ulceration which extended into the muscularis, the surface of which was necrotic and infiltrated with polymorphonuclear leukocytes (fig. 4). The submucosa and muscularis were heavily infiltrated with lymphocytes and plasma cells. The muscle bundles in many places were indistinguishable. A moderate number of eosinophils were scattered about, and Dorothy Reed cells were seen (fig. 5). Lymphoid cells showed a moderate number of mitoses.

Pathologic Diagnosis. A diagnosis of lymphogranulomatosis of the stomach with ulceration was made.

COMMENT

Of the 7 patients in the cases discussed by Singer,² 2 died incidentally to the operation. The remaining 5 patients had survived without apparent recurrence of disease for periods varying from a few months to four years. From the survival of these 5 patients Singer concluded that the prognosis is good in cases of isolated lymphogranulomatosis of the stomach after surgical removal.

In 1935, Comando³ reported a case of Hodgkin's disease of the stomach after failing to find a case in the literature since Singer's resume. Comando's patient recovered promptly from a subtotal gastrectomy and was well five years later. Comando agreed with Singer that the prognosis is good if resection is done.

Since Comando's report I have found 1 additional case reported by Imai.⁴ This case is interesting and demands close consideration.

3 Comando H N. Primary Isolated Lymphogranulomatosis of the Stomach. Arch Surg 30:228 (Feb) 1935.

4 Imai M. Primary Lymphogranulomatosis of the Stomach. J Orient Med 23:113 (Dec) 1935.

The patient was a 66 year old man who was operated on for gastric carcinoma. A lesion was found confined to the stomach, and careful exploration revealed all the other abdominal viscera to be normal. A subtotal gastrectomy was done. Microscopic examination of the resected stomach showed the typical histologic picture of Hodgkin's disease. The patient died two years later, and at postmortem examination a mass was found in the transverse colon, at the hepatic flexure. Microscopically this mass was typical of Hodgkin's disease and was identical with the gastric lesion removed two years previously.

This case suggests the possibility that lymphogranulomatosis is a progressive disease of the mesenchymal tissue, and a guarded prognosis must be made even after all apparently diseased tissue has been removed surgically.

All authors of reported cases have stressed the possible presence of microscopic disease unrecognized at the time of operation. That possibility was surely present in the case reported in this paper and is further emphasized by a case reported by Kamniker and Kratochwil.⁵ They operated for what appeared to be isolated Hodgkin's disease of the stomach, only to find at postmortem examination that there were multiple microscopic lesions in the liver, spleen and bone marrow.

There is nothing characteristic in the symptoms of isolated lymphogranulomatosis of the stomach. The condition in all cases reported has been diagnosed clinically either as carcinoma or as benign ulcer. Apparently the disease is confined to no age group, as it has been seen from the third to the seventh decade. When the condition is isolated in the stomach, the febrile state associated with the general forms of the disease is not present. Operation after a mistaken diagnosis will continue to be done until more facts are learned of the disease than are now known.

SUMMARY

A case of lymphogranulomatosis (Hodgkin's disease) isolated in the stomach is reported.

A brief resume of the literature is made.

The prognosis of lymphogranulomatosis of the stomach should be guarded even after surgical removal of the diseased tissue.

Diagnosis of this condition is practically impossible to make before microscopic examination of the lesion is done.

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⁵ Kamniker, K., and Kratochwil, K. Zur Lymphogranulomatose des Magens. Deutsche Ztschr. f. Chir. **247** 383, 1936.

CIRCULATION DURING SPINAL ANESTHESIA

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There is no adequate explanation for the marked fall in blood pressure which accompanies spinal anesthesia. In order to explain the mechanism by which this hypotension is developed, it would be necessary to know in detail all the changes which occur in the circulatory system. Thus far studies have shown conclusively that

1 Systolic and diastolic blood pressures usually fall to a variable degree¹

2 Sympathomimetic drugs usually either prevent the fall or produce a subsequent rise of blood pressure²

3 There is a rise in cutaneous temperature of the lower extremities³

Beside these definite findings, Webb, Scheinfeld and Colin⁴ reported that there was no significant variation in circulation time during spinal anesthesia in the 6 patients they studied.

We investigated the effect of spinal anesthesia on blood volume, venous pressure, circulation time, viscosity of the blood and cardiac output and its related functions.

From the Richard Morton Koster Research Laboratory, the Crown Heights Hospital.

1 Bradshaw, H. H. The Fall in Blood Pressure During Spinal Anesthesia. *Ann Surg* **104** 41 1936.

2 Babcock, W. W. Spinal Anesthesia. An Experience of Twenty-Four Years. *Am J Surg* **5** 571 1928. Evans, C. H. Possible Complications with Spinal Anesthesia, *ibid* **5** 581 1928. Crosgrove, S. A. Spinal Anesthesia in Obstetrics, *ibid* **5** 602, 1928. Albee, F. H. Spinal Anesthesia in Orthopedic Surgery, *ibid* **5** 608, 1928. Jeck, H. S. Spinal Anesthesia in Kidney and Ureteral Operations, *ibid* **5** 611 1928. Case, I. T. Lumbar Anesthesia. Remarks Based on Eleven Hundred Cases, *ibid* **5** 615 1928. DeCoursey, I. L. Newer Methods of Controllable Spinal Anesthesia, *ibid* **5** 620, 1928.

3 Scott, W. J. M. and Morton, J. I. Differentiation of Peripheral Arterial Spasm and Occlusion in Ambulatory Patients. *I. A. M. A* **97** 1212 (Oct 24) 1931.

4 Webb, G., Scheinfeld, W. and Colin, H. The Importance in Surgery of the Blood Circulation Time. *Ann Surg* **104** 460 1936.

METHOD

The subjects of these studies were surgical patients operated on for a variety of conditions. Control studies were made under similar conditions on patients, convalescents and volunteers to determine the effect of intervals without spinal anesthesia.

In each experiment the changes in circulatory phenomena were determined by observations made immediately before and during spinal anesthesia. The anesthetic was administered through a spinal puncture between the second and the third lumbar vertebra after procaine hydrochloride had been thoroughly mixed with 4 cc of cerebrospinal fluid.⁵ No sympathomimetic or other medication was used to prevent a fall in blood pressure. The dose of procaine hydrochloride was 150 mg except as otherwise indicated in the tables.

Blood volume was determined by Smith's⁶ modification of the brilliant vital red method, which permitted repetition within a short time.

The venous pressure was measured by the direct method⁷ at the time of one of the venous punctures in 7 patients of the previous group. A graduated L tube was attached to a 16 gage needle which had been inserted in the antecubital vein. The point of the needle was adjusted to a fixed portion of the patient's torso, which was marked with tincture of iodine. This procedure was followed in order to avoid difficulty in leveling two widely separated points, the arm and the base of the sternum, as is the usual practice. Our data on venous pressure are therefore relative.

The circulation time from the antecubital vein to the medulla was measured by the sodium cyanide method of Robb and Weiss.⁸

The cardiac output and its related functions were determined by the acetylene method of Grollman.⁹ The two determinations were completed within one hour under similar conditions. The control subjects were not studied under basal conditions, since we were interested only in checking the effect of repetition of the experiment after a short interval. All of the observations on cardiac output, oxygen consumption and pulse rate were completed before the start of the operation.

It will be seen from the tables that in no instance were all the data obtained from the same patient, as this was found to be impracticable. All the measurements of

5 Koster, H. Spinal Anesthesia, with Special Reference to Its Use in Surgery of the Head, Neck and Thorax, *Am J Surg* 5:554, 1928.

6 Smith, H. P. Repeated Determination of Blood Volume at Short Intervals by Means of the Dye Method, *Am J Physiol* 51:221, 1920.

7 Moritz, F., and von Tabora, D. Ueber ein Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, *Deutsches Arch f klin Med* 98:475, 1910.

8 Robb, G. P., and Weiss, S. Method for Measurement of Velocity of Pulmonary and Peripheral Venous Blood Flow in Man, *Am Heart J* 8:650, 1933.

9 Grollman, A. Cardiac Output of Man in Health and Disease, Springfield Ill., Charles C Thomas, Publisher, 1932.

venous pressure were on patients in whom blood volume had been studied, and six of the ten measurements of cardiac output, oxygen consumption and pulse rate were made together with estimation of the circulation time

RESULTS

The data are shown in the tables and summarized in table 3. The significance of the changes was calculated according to the method of Fisher¹⁰

TABLE 1—*Changes of Blood Volume and Venous Pressure During Spinal Anesthesia*

Control Observations							
Experiment	Blood Volume Liters			Difference %	Venous Pressure Cm		
	Observation		Difference		Observation		
	I	II			I	II	
9	5.63	5.78	+ 2.6	6.8	7.2	-0.4	
10	5.88	5.23	-11.7	11.4	10.5	-0.9	
11	5.34	5.57	- 4.2	9.5	8.6	-0.9	
12	5.58	5.98	- 6.9	11.8	12.2	-0.4	
14	4.65	4.68	- 0.6	12.8	11.2	-1.6	
16	3.66	3.64	- 0.5				
17	6.04	6.17	- 1.3	17.4	16.8	-0.6	
18	3.70	3.22	-13.8	23.0	24.2	-1.2	
Mean difference			-1.3 ± 1.46			-0.3 ± 0.23	

Experiments									
Experiment	Blood Volume Liters			Venous Pressure Cm			Blood Pressure Mm		
	Before	After	Change %	Before	After	Change	Before	After	Change
13	5.27	4.64	-11.9	20.2	14.8	-5.4	110	29	-81
1	5.98	4.46	-25.2	9.8	5.4	-4.4	95	45	-50
7	5.24	3.71	-29.1	5.2	4.2	-1.0	128	60	-68
5	7.05	5.75	-18.5	5.8	4.0	-1.8	85	60	-25
4	7.74	7.10	-8.4				78	60	-18
2	5.16	4.95	-4.0				108	70	-38
6	5.96	5.94	-0.3	8.0	6.8	-1.2	80	68	-12
3	4.17	4.28	+ 2.6	7.6	11.2	+3.6	93	69	-24
15	4.41	4.55	+ 3.2				101	6	-95
19	3.84	3.97	+ 3.4	16.4	15.4	-1.0	108	70	-38
8	3.53	3.73	+ 5.7				115	88	-27
20	4.05	4.56	+12.6	20.0	17.0	-3.0	92	66	-26
17	6.12	7.08	+16.7	16.8	14.2	-2.6	90	72	-18
Mean change			-4.17 ± 2.0			-1.0 ± 0.59			

SUMMARY

The average of systolic and diastolic blood pressures fell in 59 of 60 cases. This is in agreement with previous reports of the fall in blood pressure during spinal anesthesia.

10 Fisher R. A. Statistical Methods for Research Workers, ed 6. Edinburgh: Oliver & Boyd, 1936.

TABLE 2—Changes in Viscosity of the Blood

Control Observations				Experiments						
Relative Viscosity, Sec				Relative Viscosity, Sec				Blood Pressure, Mm		
Experiment	Observation		Difference	Experiment	Before	After	Change	Before	After	Change
	I	II								
70	80	80	00	70	80	79	-01	118	65	-53
71	76	76	00	71	76	75	-01	110	80	-30
72	76	76	00	72	76	76	0	95	60	-35
73	74	74	00	73	74	74	0	75	23	-52
74	74	76	+02	74	75	77	+02	120	70	-50
75	70	72	+02	75	71	67	-04	115	45	-70
76	68	70	+02	76	69	68	-01	100	68	-32
77	72	74	+02	77	73	72	-01	105	80	-25
78	78	78	00	78	78	77	-01	103	70	-33
79	72	74	+02	79	73	73	0	95	72	-23
80	80	78	-02	80	79	79	0	115	102	-13
81	74	76	+02	81	75	76	+01	110	97	-13
Mean difference			+0.05 ± 0.05	Mean change			-0.05 ± 0.04			

TABLE 3—Changes in Circulation Time

Control Observations				Experiments						
Circulation Time, Sec				Circulation Time, Sec				Blood Pressure, Mm		
Experiment	Observation		Difference	Experiment	Before	After	Change	Before	After	Change
	I	II								
21	16.5	17.0	+0.5	21	18.2	25.5	+7.3	117	75	-32
22	11.2	12.8	+1.6	22	12.0	25.0	+13.0	120	75	-45
23	9.5	9.6	+0.1	23	9.6	22.4	+12.8	105	75	-30
24	13.2	15.0	+1.8	24	14.1	28.2	+14.1	120	65	-55
25	12.2	13.4	+1.2	25	12.8	20.6	+7.8	94	92	-2
27	11.2	13.0	+1.8	26	22.0	23.4	+1.4	105	75	-30
28	13.5	12.0	-1.5	27	12.1	44.3	+32.2	134	65	-69
29	20.0	21.0	+1.0	28*	12.8	28.0	+15.2	103	68	-35
31	12.0	11.4	-0.6	29	20.5	30.2	+9.7	123	70	-53
32	15.0	14.0	-1.0	30*	14.0	24.0	+10.0	108	75	-33
33	12.4	15.0	+2.6	31	11.7	20.0	+8.3	100	75	-25
34	15.0	19.8	+4.8	32	14.5	24.1	+9.6	105	65	-40
35	7.0	6.8	-0.2	33	13.7	21.4	+7.7	95	75	-20
37	9.0	9.0	0.0	34*	17.4	18.0	+0.6	70	55	-15
38	10.4	10.6	+0.2	35†	6.9	11.0	+4.1	95	100	+5
39	11.0	15.0	+4.0	36*	26.0	24.6	-1.4	118	90	-28
40	13.2	15.8	+2.6	37*	9.0	21.0	+12.0	90	83	-7
41	10.0	12.0	+2.0	38*	10.5	49.0	+38.5	108	65	-43
42	15.0	15.0	0.0	39*	13.0	15.4	+2.4	98	90	-8
				40*	14.5	25.0	+10.5	95	70	-25
				41	11.0	15.0	+4.0	88	70	-18
				42	15.0	21.0	+6.0	95	65	-30
				43	14.0	28.0	+14.0	125	55	-70
				47	11.4	25.2	+13.8	93	55	-38
				48A†	18.0	20.2	+2.2	120	85	-35
				49†	13.4	24.0	+10.6	120	113	-7
				50	12.0	21.6	+9.6	110	68	-42
				51	20.0	26.0	+6.0	65	65	0
				53	26.0	27.2	+1.2	85	65	-20
				54	15.0	22.4	+7.4	90	63	-27
				55	11.6	24.0	+12.4	95	50	-45
Mean difference			+1.2 ± 0.25	Mean change			-0.7 ± 0.05			

* 300 mg procaine used for anesthesia
† 100 mg procaine used for anesthesia,

The pulse rate showed an average decrease of 16 beats, or 19 per cent

There was no significant change in the viscosity of the blood or in the blood volume (tables 1 and 2) The mean fall in venous pressure

TABLE 4—Changes in Cardiac Output and Related Functions

Control Observations								
Experi- ment	Oxygen Consumption Cc/Min			Cardiac Output Liters/Min				
	Observation		Differ- ence %	Observation		Differ- ence %	Cardiac Index Liters	
	I	II		I	II			
44	232	232	0.0	4.35	4.57	-4.9	2.30	
45	248	248	0.0	4.28	4.47	-4.3	2.18	
46	213	213	0.0	4.77	5.12	-7.1	2.74	
50	257	227	-12.4	3.53	4.00	-12.5	2.08	
56	193	193	0.0	4.06	4.31	-4.3	2.02	
57	205	270	-8.9	5.18	5.61	-8.0	2.85	
61	256	237	-7.9	4.52	4.35	-3.8	2.31	
62	201	206	-2.5	3.60	3.42	-5.1	1.98	
Mean difference			-3.5 ± 1.25				-1.7 ± 1.03	

Experiments													
Ex- peri- ment	Oxygen Consumption Cc/Min			Cardiac Output Liters/Min			Pulse per Min			Blood Pressure Mm			Car- diac Index Liters
	Before After		Change %	Before After		Change	Before After		Change	Before After		Change	
47	205	215	+4.8	4.81	1.82	-62	86	64	-22	92	62	-30	2.50
48*	273	242	-12.1	3.17	1.88	-41	74	80	+6	92	64	-28	1.82
48A*	247	242	-2.0	3.12	2.25	-27	84	72	-12	120	85	-35	1.72
49	3.6	348	-7.8	4.06	4.75	-5	96	84	-12	120	112	-8	2.67
53	233	242	+3.8	3.73	3.12	-16	68	48	-20	85	65	-20	2.14
54	169	170	+0.5	4.39	2.64	-21	84	60	-24	90	62	-28	3.06
55	184	184	0	4.39	1.87	-55	96	60	-36	95	80	-15	2.38
58	171	182	+6.2	3.66	2.45	-33	90	90	0	92	82	-10	2.46
59	219	209	-4.7	4.74	3.49	-26	82	76	-6	85	85	-13	3.00
60	239	220	-4.3	6.03	3.78	-37	96	72	-24	142	75	-67	3.24
Mean change			-1.06 ± 1.16	-32.3 ± 3.45			-16 ± 4.4						

* 100 mg procaine hydrochloride used for anesthesia

TABLE 5—Statistical Significance of the Difference Between the Deviations of the Control and the Experimental Observations

	Mean of the Differences Between Control Observations	Mean of the Changes After Spinal Anesthesia	Difference = Probable Error of the Difference	Probability That Difference is Not Due to Sampling %
Viscosity	-0.08 ± 0.05	-0.05 ± 0.025	-0.13 ± 0.09	6
Blood volume	-1.3 ± 1.7%	-4.17 ± 2.6%	-2.87 ± 2.9%	49
Venous pressure	-0.3 ± 0.15 cm	-1.9 ± 0.90 cm	-1.6 ± 0.64 cm	91
Circulation time	-1.2 ± 0.25 sec	-9.7 ± 0.95 sec	8.5 ± 1.01 sec	100
Cardiac output	-1.7 ± 1.63%	-32.3 ± 3.6%	-34 ± 2.95%	100
Oxygen consumption	-3.3 ± 1.82%	-1.5 ± 1.21%	1.74 ± 1.75%	70

of 19 cm of saline solution has about a 90 per cent chance of being significant according to the method of calculation used in obtaining the data presented in table 5. However the occurrence in 8 of

9 anesthetized patients of the same direction of change in venous pressure (a fall) would be found only 96 per cent of the time. The data indicate, therefore, that antecubital venous pressure probably falls significantly but by an amount which has not been precisely estimated.

The circulation time from arm to brain increased 60 per cent after spinal anesthesia (table 3).

The cardiac output fell 32.3 per cent (table 4). There was no significant associated change in oxygen consumption.

CONCLUSION

A significant fall in cardiac output, pulse rate and venous pressure and an increase in circulation time from arm to brain are associated with spinal anesthesia in man.

THYROTOXICOSIS WITH MALIGNANT NEOPLASMS OF THE THYROID GLAND

A CLINICOPATHOLOGIC STUDY

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The incidence of malignant disease of the thyroid gland is low. Various observers have shown that it does not rise much above 1 per cent for all autopsies. Wilson¹ estimated its occurrence at 0.11 per cent, Hinterstoisser² at 0.27 per cent and Wegelin³ at 1.04 per cent. In spite of considerable study (von Eiselsberg,⁴ Langhans,⁵ Kocher,⁶ Trotter,⁷ Klose and Hellwig,⁸ Rogers,⁹ Meleney,¹⁰ Carrel,¹¹ Speese and Brown,¹² Bloodgood,¹³ Balfour,¹⁴ Simpson,¹⁵ Wilson,¹ Ewing,¹⁶

From the Department of Surgery, the University of Tennessee School of Medicine.

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10 Meleney, F. L. A Metastasizing Malignant Tumour of the Thyroid Gland, *Ann Surg* **76** 684-694, 1922.

11 Carrel, A. Du cancer thyroïdien quelques considerations sur son etiology et sa physiologie pathologique. *Gaz d hop* **73** 713-720, 1900.

12 Speese, J., and Brown, H. P., Jr. Malignant Degeneration of Benign Tumors of the Thyroid Gland, *Ann Surg* **74** 684-690, 1921.

13 Bloodgood, J. C. Adenoma of the Thyroid Gland. A Clinical and Pathological Study, *Surg, Gynec & Obst* **2** 121-144, 1906.

14 Balfour, D. C. Cancer of the Thyroid Gland. *M Rec* **94** 846-850, 1918.

15 Simpson, W. M. A Clinical and Pathological Study of Fifty-Five Malignant Neoplasms of the Thyroid Gland. *Ann Clin Med* **4** 643-667, 1925.

16 Ewing, J. Neoplastic Diseases. Philadelphia, W. B. Saunders Co., 1928, pp. 956-961.

Graham¹⁷). the diagnosis of malignant disease of the gland, both clinical and histologic, remains difficult. The disease in at least one third of the cases is diagnosed incorrectly prior to operation, and it is probable that the condition frequently is unrecognized even after operative exposure. Hitherto the pathologic study of malignant neoplasms of the thyroid gland has been conducted from the morphologic point of view. It is possible that a study of these growths from the standpoint of function may lead to some simplification of the problems involved. Accordingly, this study has been undertaken with the object of focusing attention on the types of malignant thyroid tumor accompanying thyrotoxicosis. Furthermore, since this thyrotoxicosis appears to be truly thyrogenic, such an investigation may help to throw light on the problem of thyroid function in general.

FUNCTIONING OF MALIGNANT THYROID NEOPLASMS

The possibility of function occurring in malignant disease of the thyroid gland probably had been thought of many years before the time of von Eiselsberg. However, no observation of importance had been made until von Eiselsberg's case⁴ was reported in the literature. In 1881 Tillaux¹⁸ reported a case of sarcoma of the thyroid gland in which symptoms of thyrotoxicosis were present. This is the only case of thyrotoxicosis with sarcoma of the thyroid which has been verified. Many other writers have reported the occurrence of sarcomas of the gland with toxic symptoms, but their reports have not been substantiated. After this, a London physician, Dr G. Gulliver,¹⁹ read before the Pathological Society of London the report of a case of malignant disease of the thyroid gland in which myxedema had occurred. Two schools of thought now sprang up, the German and the French. The German school, founded by von Eiselsberg, was filled, up to the close of the nineteenth century, with such physicians as Harmer,²⁰ von Rehn,²¹ Mosler,²² Hurthle²³ and Lucke²⁴. Little was done by the French school

17 Graham, A. Malignant Epithelial Tumours of the Thyroid, with Special Reference to Invasion of Blood Vessels, Surg, Gynec & Obst **39** 781-790, 1924.

18 Tillaux, P. J. Sarcome du corps thyroïde, Bull et mem Soc de chir de Paris **7** 698-712, 1881.

19 Gulliver, G. Malignant Disease of the Thyroid from a Case of Myxoedema, Tr Path Soc London **37** 511-513, 1885-1886.

20 Harmer, L. Schilddrusencarcinommetastase in der Nasenhöhle, Wien klin Wchnschr **12** 628-631, 1899.

21 von Rehn, L. Die chirurgische Behandlung des Morbus Basedown, Mitt a d Grenzgeb d Med u Chir **7** 165-182, 1900-1901.

22 Mosler, F. Rechtsseitiger Tumor der Glandula thyroidea mit secundärem Exophthalmos, Deutsche med Wchnschr **16** 794, 1890.

23 Hurthle, O. Beiträge zur Kenntnis des Sekretionsorganges in der Schilddrüse, Arch f Physiol **56** 1-44, 1894.

24 Lucke, A. Cancroid der Schilddrüse mit sehr akutem Verlauf, Arch f klin Chir **8** 88-93, 1867.

by the end of the nineteenth century, for Tillaux¹⁸ was followed only by Bertrand,²⁵ who wrote in 1896 a thesis on acute and latent cancer of the thyroid

In the first decade of the twentieth century an outburst of activity took place in France, and the writings of Faisant,²⁶ Berard,²⁷ Carrel¹¹ Hebert,²⁸ Berard and Alamartine,²⁹ Broeckaert³⁰ and Delore and Alamartine³¹ found a place in the literature. Meanwhile, in Germany, Stejskal,³² Hirschfeld,³³ Caro,³⁴ Lowy,³⁵ Lobenhoffer³⁶ and Gierke³⁷ were active. The work of Marine and Johnson³⁸ exerted a profound influence on the German school but practically none on the French. A scientific study was now initiated in Germany of the problem of function in malignant neoplasms of the thyroid gland (Mori,³⁹ Ewald,⁴⁰ Lyon,⁴¹

25 Bertrand, P. *Formes aiguës et formes latentes du cancer thyroïdien*, Thesis, Lyon, 1896

26 Faisant, M. *Neoplasme thyroïdien greffe sur un goitre ancien avec hyperthyroïdisation*, *Lyon med* **105** 1019-1021, 1905

27 Berard, L. *Thyroidectomie subtotale pour cancer thyroïdien*, *Lyon med* **114** 471-474, 1910

28 Hebert, P. *Fibrome de la glande thyroïde et syndrome basedowien*, *Bull et mem Soc anat. de Paris* **79** 843-848, 1904

29 Berard, L., and Alamartine, H. *Une forme latente du cancer thyroïdien*, *J med franç* **2** 32-40, 1908

30 Broeckaert, M. *Goitres et cancers thyroïdiens exophthalmiques*, *Presse med* **19** 4, 1911

31 Delore, X., and Alamartine, H. *Cancer massif du corps thyroïde avec basedowisme. Hemithyroidectomie de decompression, myxoedème post-opératoire*, *Lyon med* **115** 141-148, 1910

32 Stejskal, H. *Hyperthyreoidismus bei multiplen Tumoren*, *Deutsche med Wchnschr* **34** 359-362, 1908

33 Hirschfeld, R. *Zur Pathogenese des Basedowschen Symptomenkomplexes*, *Zentralbl f Nervenh* **29** 832-835, 1906

34 Caro, L. *Zur Pathogenese der Schilddrüsenerkrankungen*, *Wien klin Rundschau* **20** 361, 1906

35 Lowy, I. *Ueber Basedowsymptome bei Schilddrüsenneoplasmen*, *Wien klin Wchnschr* **22** 1671-1676, 1909

36 Lobenhoffer, O. *Beiträge zur Lehre der Sekretion in der Struma*, *Mitt a d Grenzgeb d Med u Chir* **20** 650-662, 1909

37 Gierke, H. *Ueber Knochentumoren mit Schilddrüsenbau*, *Virchows Arch f path Anat* **170** 464-501, 1902

38 Marine, D., and Johnson, A. A. *Experimental Observations on the Effects of the Administration of Iodin in Three Cases of Thyroid Carcinoma (Two Human and One Canine)*, *Arch Int Med* **11** 288-299 (March) 1913

39 Mori, T. *Ueber das Auftreten thyreotoxischer Symptome bei Geschwulst-anomalien in der Schilddrüse*, *Frankfurt Ztschr f Path* **12** 2-24, 1913

40 Ewald, K. *Ueber den Jodgehalt des Adenocarcinomas der Schilddrüse und seiner Metastasen*, *Wien klin Wchnschr* **9** 186, 1896

41 Lyon, E. *Ueber einen Fall von Zylinderzellencarcinom der Schilddrüse bei Basedowscher Krankheit*, *Ztschr f Krebsforsch* **14** 501-525, 1914

Meyer-Hurlmann and Oswald,⁴² Erdheim,⁴³ Branovacky,⁴⁴ Lublin,⁴⁵ Hoffmann,⁴⁶ Winkler,⁴⁷ Stange,⁴⁸ and others) In France, Pallasce and de Lambert⁴⁹ have written on this subject, in English speaking countries, Eisen,⁵⁰ Simpson,⁵¹ Kolodny⁵¹ and Crile,⁵² and in Italy, Pescatori⁵³

The theory held by the German school is that the thyrotoxic symptoms are due not to functioning of the malignant growth itself but to stimulation of the thyroid tissue surrounding the primary growth. That held by the French school, on the other hand, is that the toxic symptoms are the result of actual function of the malignant cells. Of course, it need scarcely be stated that not all adherents of each school take the central point of view of that school, for many favor some modification of it.

That thyrotoxicosis does accompany malignant neoplasms of the thyroid gland is generally acknowledged. Many writers have described cases of primary tumor of the gland with toxic symptoms (Lowy,³⁵

42 Meyer-Hurlmann, S., and Oswald, A. Karzinom der Schilddrüse mit exzessiver spezifischen Drüsensfunktion, *Cor-Bis f. Schweiz. Aerzte* **43** 1468-1473, 1913

43 Erdheim, S. Anatomische und klinische Untersuchungen über Primärgeschwulste vortauschende Metastasen, insonderheit solcher des Adenocarcinoms des Schilddrüse, *Arch. f. klin. Chir.* **117** 274-317, 1921

44 Branovacky, M. Die biologische Wirksamkeit verschiedener Kropffarten im Kaulquappenversuch, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **39** 563-592, 1926

45 Lublin, A. Neuere klinische Beobachtungen bei Thyreotoxikosen, *Ztschr. f. klin. Med.* **114** 33-78, 1930

46 Hoffmann, P. Metastases of Ovarian Carcinoma with Symptoms of Basedow's Disease, *Bratisl. lekar. listy* **11** 207-213, 1931

47 Winkler, W. Ueber Hypothyreodismus bei metastatischem Carcinom der Schilddrüse, *Ztschr. f. klin. Med.* **120** 400-407, 1932

48 Stange, G. Thyreotoxikose bei Hypernephrommetastasen in der Schilddrüse, *Inaug. Dissert.*, Frankfurt, 1924-1925

49 Pallasce, S., and de Lambert, P. *Forme medicale du cancer thyroïdien*, *Lyon med.* **130** 302-303, 1921

50 Eisen, D. Malignant Tumors of the Thyroid. An Analysis of Seven Cases with a Study of the Structure and Function of the Metastases, *Am. J. M. Sc.* **170** 61-74, 1925

51 Kolodny, A. Hypernephroma of the Thyroid, with a Clinical Picture of Exophthalmic Goiter, *Arch. Path.* **1** 37-40 (Jan.) 1926

52 Crile, G., Jr. Hyperthyroidism Associated with Malignant Tumors of the Thyroid Gland, *Surg., Gynec. & Obst.* **62** 995-999, 1936

53 Pescatori, F. Le alterazioni del miocardio in due casi di gravi affezioni tiroidee, morbo di Basedow e adenocarcinoma della tiroide, *Endocrinol. e pat. costit.* **3** 187-200, 1928

Ehrhardt,⁴ Boeckel,⁵ Haemig,⁶ Harmer,⁷⁰ Cornil,⁵⁷ Kocher,⁵⁸ Hebert,⁵⁸ Clunet,⁵⁸ Gillaux,⁵¹ Lyon,⁴¹ Broekaert,⁵⁰ Meyer-Hurlmann and Oswald,⁴² Klose and Hellwig and others.) In view of these reports extending over half a century, the existence of thyrotoxicosis with malignant neoplasms of the thyroid gland cannot be doubted. The criteria used by various workers in their determination of the thyrotoxic state have varied greatly.

How are the thyrotoxic symptoms produced? What is the mechanism of their production in primary and secondary malignant disease of the thyroid gland?

- 1 The toxic symptoms associated with primary tumors may be due to
 - (a) Functioning of the malignant neoplastic tissue
 - (b) Basedowification of the thyroid tissue surrounding the malignant mass by
 - (1) Toxic substances from the growth
 - (2) Mechanical irritation of the neoplasm
 - (c) Absorption or hyperabsorption of normal colloid which has been set free from acini invaded by the neoplasm
 - (d) Absorption or hyperabsorption of altered colloid or colloid from abnormal acini
- 2 The toxic symptoms associated with secondary tumors may be due to any of the factors *b*, *c* or *d* active in the case of primary tumors
- 3 Thyrotoxicosis may occur from thyroid metastases (Lown,³² Stejskal³²)
- 4 Thyrotoxicosis may occur from thyroid ectopias (Kovacs,⁵⁹ Moench⁶⁰)

54 Ehrhardt, O. Zur Anatomie und Klinik der Struma maligna, Beitr. z. klin. Chir. **35** 343-464, 1902

55 Boeckel, E. Goitre sarcomateux enorme, Gaz. d. hop. **57** 1100-1101 1884

56 Haemig, G. Anatomische Untersuchungen über Morbus Basedow. Arch. f. klin. Chir. **55** 1-68, 1897

57 Cornil, V. Epithelioma du corps thyroïde, Compt. rend. Soc. de biol. **2** 273-280, 1875

58 Clunet, J. Accidents cardiaques au cours d'un cancer thyroïdien. Arch. d. mal. du cœur **1** 232-245, 1908

59 Kovacs, F. Ueber die Schilddrüsengeschwulst des Ovariums. Arch. f. Gynak. **122** 766-777, 1924

60 Moench, G. L. Thyroid Tissue Tumours of the Ovary with Report of an Apparently Toxic Case, Surg., Gynec. & Obst. **49** 150-159 1920

TRUE AND FALSE THYROTOXICOSIS

In distinguishing true from false thyrotoxicosis it is dangerous to stress the importance of a single sign or symptom. For instance, it is common to evaluate too highly the basal metabolic rate, in spite of contradictory clinical evidence. Hypermetabolism per se is not thyrotoxicosis. In all forms of malignant disease the metabolic rate is usually raised as high as +10 to +40 per cent (Grafe,⁶¹ Du Bois,⁶² Strieck and Mulholland,⁶³ Kraus,⁶⁴ Wallersteiner,⁶⁵ Magnus-Levy⁶⁶) Heindl and Trauner⁶⁷ in an examination of material from the von Eiselsberg clinic established that in patients with cancer the basal metabolic rate may be raised to +40 per cent.

ANALYSIS OF PRESENT SERIES

The present study concerns a group of 50 cases, in all of which operation was performed and tissue was removed from the thyroid gland. Malignant disease of the gland was suspected or definitely diagnosed prior to operation in about one third of these cases. In every case a microscopic diagnosis of malignant neoplasm of the thyroid gland was made.

Sex Incidence—Of the 50 patients, 40 were females and 10 males—a ratio of 4 to 1.

Age Incidence—A study of the age incidence revealed several interesting facts. The average age for the entire group was 47 years, and there was a gross variation from a minimum of 7 to a maximum of 72 years. A subdivision of the entire series into two groups, those with and those without thyrotoxicosis, was made. In chart 1 is illustrated the relative age incidence in each group. The maximum age incidence of the nontoxic group lies, like that of the total series, between 40 and 50 years. Thyrotoxicosis, on the other hand, reached its peak in patients between 50 and 60 years of age. It is difficult at present to explain this variation in age incidence between the different groups.

61 Grafe, E. *Die Pathologie und Physiologie des Gesamtstoffwechsels*, Munich, J. F. Bergmann, 1922.

62 Du Bois, E. F. *Basal Metabolism in Health and Disease*, Philadelphia, Lea & Febiger, 1923.

63 Strieck, F., and Mulholland, H. B. *Untersuchungen über den Gaswechsel bei Kranken mit malignen Tumoren*, *Deutsches Arch f klin Med* **162** 51-67, 1928.

64 Kraus, F. *Ueber das Kropfherz*, *Wien klin Wchnschr* **12** 416-421, 1899.

65 Wallersteiner, E. *Untersuchungen über das Verhalten von Gesamtstoffwechsel und Eisweissumsatz bei Carcinomatosen*, *Deutsches Arch f klin Med* **116** 145-187, 1914.

66 Magnus-Levy, A. *Der Einfluss von Krankheiten auf den Energiehaushalt im Ruhezustand*, *Ztschr f klin Med* **60** 177-224, 1906.

67 Heindl, A., and Trauner, R. *Der Grundumsatz von Karzinomkranken*, *Mitt a d Grenzgeb d Med u Chir* **40** 416-432, 1927.

Incidence of Thyrotoxicosis—Of the 50 patients 14 showed cleancut evidences of thyrotoxicosis, an incidence of 28 per cent. Other observers (e. g., Simpson¹⁰) have found a higher incidence of thyrotoxic symptoms in such cases, placing it in the neighborhood of 50 per cent. This may be explainable by the wide variation in criteria used in the diagnosis of thyrotoxicosis by many investigators. Of the 10 male patients in this series not one revealed any thyrotoxic symptoms.

Duration of Symptoms—An unsuccessful attempt was made to determine whether any relation existed between the duration of the thyrotoxic symptoms and the metabolic rate. It was noted, however, that the patient with the shortest duration of thyrotoxicosis (one month) had a

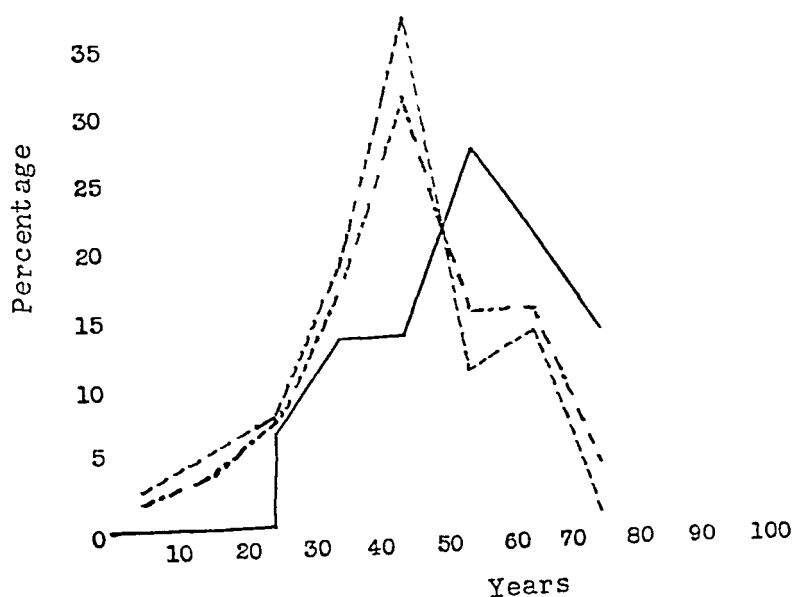


Chart 1—Age incidence. The figures at the bottom of the chart represent the age range, those at the left, the percentage. The unbroken line represents the thyrotoxic group, the broken line, the nontoxic group, the line composed of dots and dashes, the total incidence.

metabolic rate of +63 per cent, the highest in this group. The duration of thyrotoxicosis varied from one month to twelve years (chart 2). It seems unlikely that a malignant neoplasm could have existed in the thyroid gland for twelve years. One must assume, therefore, that the neoplasm developed in a hypert functioning gland. In chart 3 is shown the relative duration of goiter of the toxic and the nontoxic type. Goiter of less than two years' duration more frequently was toxic (33 per cent) than nontoxic (19 per cent). In 50 per cent of cases of thyrotoxicosis it had been present for one year or less, while in more than 70 per cent its duration did not exceed two years.

and vesicular nuclei. This type of growth probably corresponds to the Hurthle type of carcinoma. In many of the neoplasms gross hemorrhages could be found. From table 1 it can be seen that hemorrhage apparently is more frequent with toxic than with nontoxic goiter. It is not possible as yet to state the exact reason for this. A search was made in the thyroid glands, both in the neoplasm and in the surrounding thyroid tissue, for evidences of regenerative hyperplasia. This type of

TABLE 1—*Thyrotoxicosis Relation to Intraneoplastic Hemorrhage*

Thyrotoxic group (11 cases) Hemorrhage	Nonthyrotoxic group (36 cases) Hemorrhage
1 Papillary adenocarcinoma, grade 1	1 Carcinoma, grade 4
2 Adenocarcinoma, grade 2	2 Adenocarcinoma, grade 2
3 Adenocarcinoma, grade 2	3 Papillary adenocarcinoma, grade 1
4 Adenocarcinoma, grade 3	4 Squamous cell epithelioma, grade 4
5 Papillary adenocarcinoma, grade 1	5 Carcinoma, grade 4
6 Adenocarcinoma, grade 2	6 Adenocarcinoma, grade 2
7 Adenocarcinoma, grade 1	7 Papillary adenocarcinoma, grade 1
8 Adenocarcinoma, grade 2	
9 Carcinoma, grade 3	No hemorrhage
10 Adenocarcinoma, grade 2	1 Carcinoma, grade 4
11 Adenocarcinoma, grade 2	2 Adenocarcinoma, grade 2
12 Carcinoma, grade 2	3 Papillary adenocarcinoma, grade 1
No hemorrhage	4 Carcinoma, grade 2
1 Carcinoma, grade 4	5 Carcinoma, grade 2
2 Papillary adenocarcinoma, grade 1	6 Adenocarcinoma, grade 2
	7 Carcinoma, grade 4
	8 Papillary adenocarcinoma, grade 1
	9 Adenocarcinoma, grade 2
	10 Papillary adenocarcinoma, grade 2
	11 Carcinoma, grade 3
	12 Adenocarcinoma, grade 3
	13 Papillary adenocarcinoma, grade 1
	14 Adenocarcinoma, grade 3
	15 Adenocarcinoma, grade 1
	16 Adenocarcinoma, grade 1
	17 Adenocarcinoma, grade 2
	18 Carcinoma, grade 4
	19 Adenocarcinoma, grade 4
	20 Carcinoma, grade 3
	21 Carcinoma, grade 3
	22 Carcinoma, grade 2
	23 Adenocarcinoma, grade 3
	24 Carcinoma, grade 4
	25 Adenocarcinoma, grade 1
	26 Fibrosarcoma, grade 3
	27 Squamous cell epithelioma, grade 3
	28 Adenocarcinoma, grade 1
	29 Carcinoma, grade 1

hyperplasia was found in varying degrees from a few scattered regenerative hyperplastic cells to extensive areas of regenerative hyperplasia. Regenerative hyperplasia was more common and more extensive in neoplasms of low grade malignancy than in the more malignant growths. In addition, it occurred more frequently in papilliferous than in non-papilliferous neoplasms. Moreover, it appeared to be less frequent with thyrotoxicosis. Whether or not there exists any true relation between the presence or absence of regenerative hyperplasia and the presence or absence of thyrotoxicosis cannot be definitely stated. However, it is my impression that such a relation does not exist.

Relation of Differentiation of Growth to Thyrotoxicosis—In every instance in which thyrotoxicosis was present structural evidences of function were found either in the neoplasm or in the surrounding thyroid tissue. In some neoplasms the malignant acini were lined with tall columnar cells and filled with pale-staining vacuolated material resembling colloid. In other instances signs of hypertunction were found not in the growth itself but in the surrounding tissue. This was particularly true when the neoplasm was more or less differentiated. Chart 5 illustrates the fact that

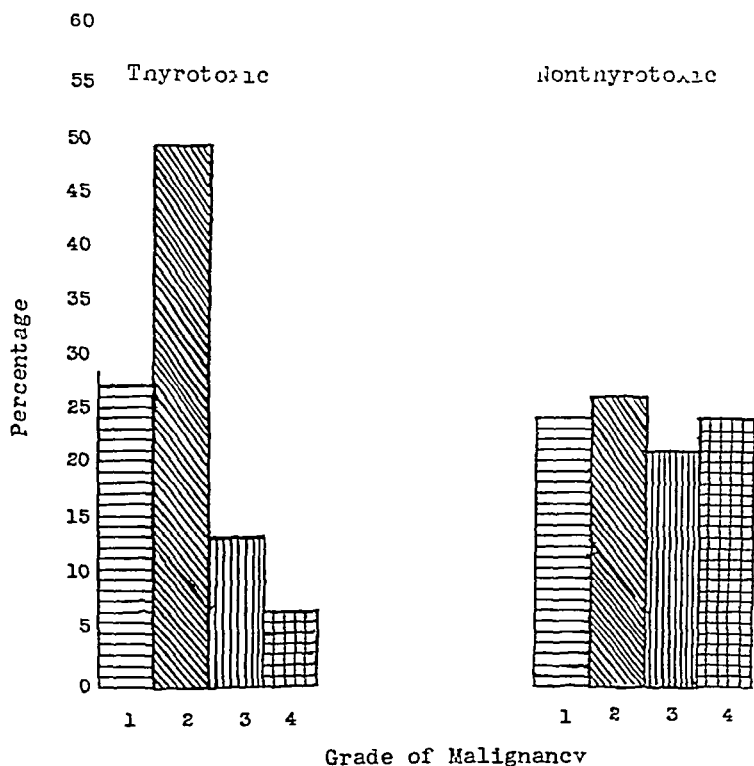


Chart 5—Thyrotoxicosis in relation to the grade of malignancy of the tumor. The figures at the bottom of the chart represent the grade of malignancy, those at the left, the percentage.

in the majority of cases of thyrotoxicosis the neoplasms are of a low grade of malignancy. These data may be interpreted in two ways. There is the possibility that well differentiated neoplasms are more capable of functioning and therefore of producing the symptoms of thyrotoxicosis. On the other hand it is possible that a neoplasm of low malignancy by its slower growth is more capable of producing a specific basedowifying effect on the surrounding thyroid epithelium. In either case the

constitutional predisposition of the thyroid gland to basedowification may be the determining factor (Klose and Hellwig,⁸ Warthin⁶⁸)

PROGNOSIS OF MALIGNANT NEOPLASMS OF THE THYROID GLAND
IN RELATION TO THYROTOXICOSIS

An examination of the rate of survival in the present series of malignant neoplasms of the thyroid gland reveals an interesting fact. Over a period of five years death from tumor occurred in 21.4 per cent of the thyrotoxic group in contrast to a death rate of 44.4 per cent in the nonthyrotoxic group. This is in agreement with the fact that the general grade of malignancy in the thyrotoxic group is lower than in the

TABLE 2—*Prognosis of Malignant Disease of the Thyroid Gland*

Neoplasm	Grade	Comment
Thyrotoxic Group (14 Cases)		
Adenocarcinoma	4	Metastases to brain
Adenocarcinoma	2	Metastases to larynx, lung
Papillary adenocarcinoma	1	Recurrent local infiltration
Nonthyrotoxic Group (36 Cases)		
Adenocarcinoma	4	Metastases to pelvis
Adenocarcinoma	2	Metastases to cervical glands
Adenocarcinoma	2	Death in 2 years
Adenocarcinoma	2	Metastases to liver and skull
Adenocarcinoma	3	Metastases to cervical glands
Adenocarcinoma	2	Metastases to supraclavicular glands
Fibrosarcoma	3	Death in 2 months
Adenocarcinoma	2	Metastases to brain, liver, spleen and cervical glands
Adenocarcinoma	2	Death in 1 year
Adenocarcinoma	3	Metastases to cervical glands, mediastinum, death in 2 ¹ / ₂ years
Adenocarcinoma	3	Metastases to lungs, death in 9 months
Adenocarcinoma	2	Local metastases, death in 4 months
Papillary adenocarcinoma	2	Metastases to parotid gland, death in 4 years
Squamous cell carcinoma	4	Death in 1 year
Adenocarcinoma	2	Metastases to supraclavicular glands and lungs, death in 1 year
Diffuse carcinoma	4	Death in 6 months

nonthyrotoxic group. The presence of thyrotoxicosis accompanying a malignant thyroid neoplasm would suggest a distinctly more favorable prognosis over a five year postoperative period (table 2).

COMMENT

Out of our analysis of this series of 50 malignant thyroid tumors several facts emerge:

1. Thyrotoxicosis seems to be more frequently associated with adenocarcinoma of low or moderate grade of malignancy than with papillary forms of carcinoma.

2. Toxic symptoms are not produced by carcinoma in which the cells are completely dedifferentiated, that is, by the most malignant type.

⁶⁸ Warthin, A. S. The Constitutional Entity of Exophthalmic Goiter and So-Called Toxic Adenoma, *Ann Int Med* 2: 553-570, 1928.

Such symptoms are also absent with growths composed of nonfunctioning cell forms, such as squamous epithelioma and fibrosarcoma

3 The cells most capable of functioning and therefore of producing thyrotoxic symptoms are the common thyroid cells of small and moderate size. The large cell forms of thyroid neoplasm seem to be somewhat less prone to cause toxicity. In the thyrotoxic group only 14 per cent of tumors showed a large cell structure, whereas in the nonthyrotoxic group 25 per cent were composed of large cells.

4 Acinus formation was present in over 70 per cent of growths accompanying thyrotoxicosis.

5 The prognosis is more favorable for malignant neoplasms of the thyroid gland with than without toxic symptoms.

SUMMARY

A series of 50 cases of malignant disease of the thyroid gland is presented.

A study has been made of the thyrotoxicosis which accompanies a certain proportion of tumors of the thyroid gland.

An analysis has been made of the structural peculiarities of the neoplasms which are accompanied by thyrotoxic states.

It is suggested that certain histologic and cytologic criteria must be fulfilled by any tumor of the thyroid before it can produce thyrotoxicosis.

EMBRYOLOGY OF THE HIP JOINT

PRELIMINARY OBSERVATIONS

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NEW YORK

AND

PAUL C COLONNA, M D

OKLAHOMA CITY

The present preliminary study of the hip joint was made on a series of embryos and fetuses collected in cases of therapeutically interrupted pregnancies of varying duration

It is felt that the majority of standard works dealing with embryology and developmental anatomy do not give sufficient information with regard to the development of the structures forming the hip joint to be of great value to the orthopedic surgeon, and this preliminary report may stimulate further work on a subject replete with data capable of practical application

METHOD

The embryo or fetus was split sagittally in the midline, after which the specimen was cut through the trunk in the horizontal plane just above the level of the hip joint. The hip joint was found to be on a level with the symphysis pubis anteriorly and at the level of the first or the second sacral segment posteriorly. Serial sections were cut just above this level in the horizontal plane and were continued through the entire thickness of the hip joint. In this way all structures were included. A few sections were lost, no attempt, therefore, has been made to perform serial reconstruction of the hip joint from serial sections, although the desirability of this method is admitted

PROTOCOLS

SPECIMEN 1 (embryo aged about 6 weeks) —This embryo was studied by means of descending horizontal serial sections starting in the midabdominal region and continuing caudally. In some sections the cartilage of the ilium appeared. It was extremely primitive both histologically and morphologically, and no definite sacroiliac joint space was present. As the sections continued through the ilium one identified what was undoubtedly the primitive hip joint. The cartilages composing it were more or less formless, but there was some evidence of rearrangement of the ilium to form a slight concavity in which the cartilage of the femur rested. The space between the two cartilages was filled with undifferentiated cellular

From the Hospital for the Ruptured and Crippled, New York, and the Crippled Children's Hospital, Oklahoma City

tissue, so that actually there was merely a suggestion of a joint space. There were no blood vessels in any of the cartilages, and the cotyloid ligament seen in the older embryos was not differentiated. There were some soft tissue buds which represented the lower limbs.



Fig 1—Sagittal section of a 6 week embryo showing the primitive hip joint. The acetabulum is to the right.

SPECIMEN 2 (embryo aged about 10 weeks).—This embryo was not split sagittally as were the larger specimens. The sections commenced at the level of the first sacral vertebra. There were beginning calcification and ossification of the center of the iliac bone but all the other structures were cartilaginous. The

sacroiliac joint appeared as a thin but well defined joint space containing blood vessels and embryonal connective tissue. The cartilages were surrounded by fibrous perichondrium composed of embryonal connective tissue, and the dorsal processes of the sacral vertebrae did not meet in the midline, the gap being bridged by connective tissue. There was a small center of ossification in the center of the body of each of the sacral vertebrae, and a small myxomatous area represented the corpus vertebrae, or the remnant of the notochord. The ossification of the iliac bone seemed to be greatest at the sacroiliac junction. As the serial sections were studied, the ilium became constricted into two portions, the anterior portion was triangular and assumed a close relation with the hip joint, as will appear in the further description. We refer to this anterior portion of the ilium as a part of the triradiate cartilage. In the further serial sections the cavity of the acetabulum appeared as a small circular space lined by flattened, condensed cartilage cells. About three fourths of the circumference was cartilaginous and one fourth was fibrous, the fibrous portions representing the primitive cotyloid ligament. The acetabular space was present before the head of the femur appeared, indicating that there was an appreciable joint width between the roof of the acetabulum and the head of the femur. The roof of the acetabulum was formed entirely by the ilium, and the triradiate cartilage was continuous with the superior ramus of the pubis. In the later sections the femoral head appeared as a club-shaped avascular cartilaginous structure. Small portions of the femoral shaft, which was partly ossified, were also observed. There was no well defined neck of the femur as seen in the older embryos, although there was a lateral protuberance corresponding to the greater trochanter. No joint capsule could be identified, the soft tissue in the vicinity being loose in arrangement. In deeper sections the ligamentum teres was encountered arising from the foveal region of the head, and it could be traced to its insertion in the acetabulum. It contained no blood supply.

Summary—In the 10 week embryo all of the pelvic structures are formed in cartilage except for a center of ossification in the portion of the iliac bone opposite the sacroiliac joint. This corresponds to the position of greatest strain. None of the cartilages show a blood supply. The head and neck of the femur are club shaped and not particularly differentiated. The trochanter, however, is differentiated. There is little vascularization of any of the structures, although there are a few blood spaces in the periphery of the acetabulum and in the fibrous tissue around the head, in the location that would correspond to the neck if it were formed. There are fibrous strands near the acetabular region and the trochanteric region, but they can scarcely be identified as a capsule such as is seen in the $4\frac{1}{2}$ month fetus. The hip joint is at the level of the symphysis pubis, but both the hip joint and the symphysis pubis seem to be at the level of the first sacral vertebra. The cotyloid ligament and the ligamentum teres are both formed. The latter does not possess a blood supply.

SPECIMEN 3 (fetus aged about 14 weeks)—The early sections above the level of the hip joint showed a somewhat larger center of ossification of the ilium than did those of the embryo previously described. When the triradiate cartilage was encountered, it was noted that around its periphery there were several blood

channels. The acetabulum first appeared as a complete circle and later as about three fourths of a circle. It was lined by fibrous perichondrium. The head of the femur was composed entirely of cartilage and was far more shapely than that of the 11 week embryo. No synovial elements could be identified in either specimen.

Summary—In the 14 week embryo the acetabulum, the femoral head and neck and the trochanter are formed of cartilage. The cotyloid liga-

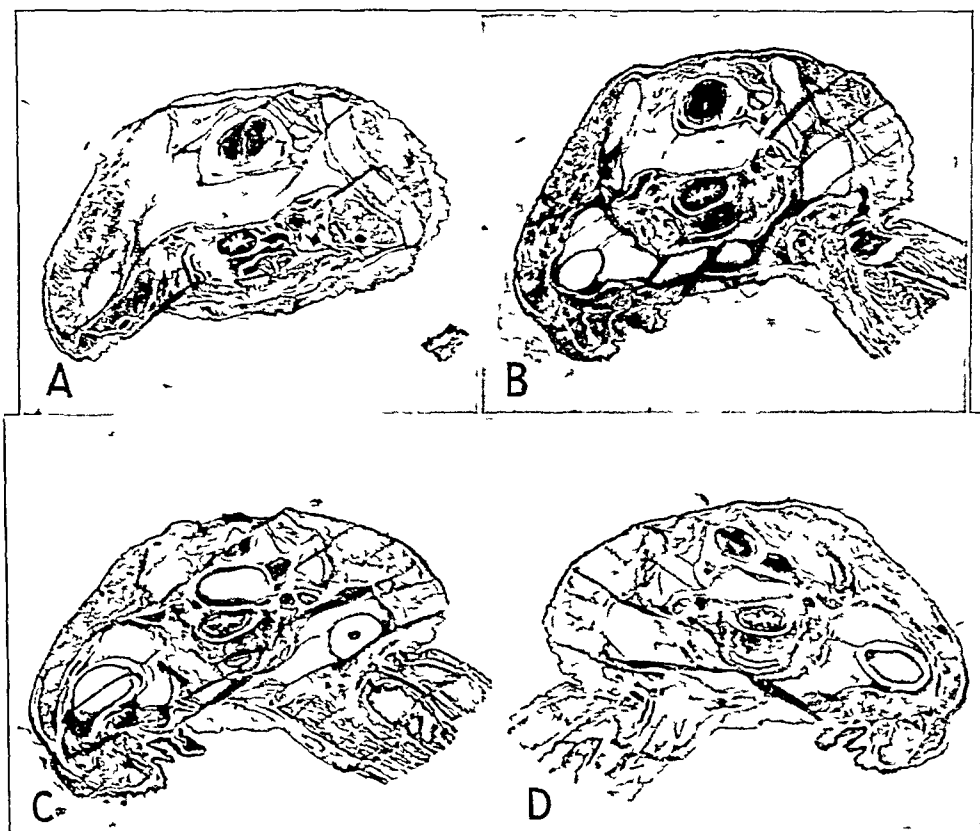


Fig 2—4 horizontal section through a 10 week embryo at the level of the sacroiliac joint. The iliac cartilage is undergoing ossification. The dorsal laminae are not fused. B, same embryo. The section shows the acetabulum on the left side at the level of the pubic symphysis anteriorly. Notice the well formed cotyloid ligaments and the absence of any blood supply to the cartilages. C same embryo. The head of the femur is flattened and club shaped. The ligamentum teres is avascular. Notice the absence of a joint capsule. D same embryo. The general features are the same. The blood supply of the head is more marked from the capsular side. The cotyloid ligaments are present.

ment and the ligamentum teres are well defined. The latter is vascular. The structures have a more nearly adult shape than the club-shaped head seen in the 10 week embryo. No well defined joint capsule is present. The fovea centralis is composed of myxomatous tissue. The head is slightly vascular, the blood vessels being near its periphery and opposite the ligamentum teres. The acetabular cartilage is sur-

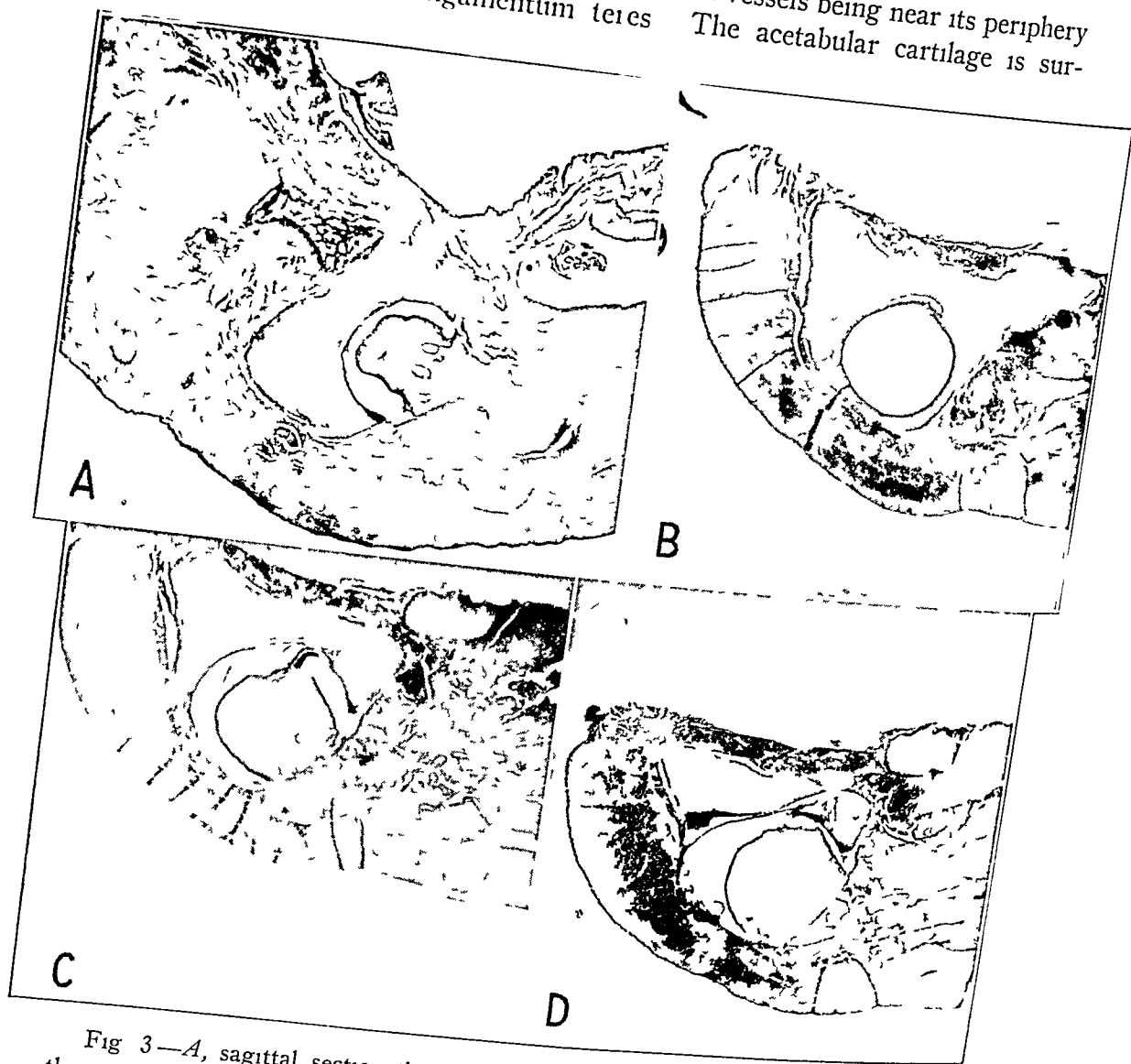


Fig 3—A, sagittal section through the hip joint of a 14 week fetus, showing the acetabulum and the ilium. Notice the blood supply of the intertrochanteric region. B, same fetus in horizontal section, showing the acetabulum and a portion of the pubic ramus. There is beginning vascularization of the acetabulum at the site of attachment of the ligamentum teres. C, same fetus, showing the head of the femur in the acetabulum. The ligamentum teres is readily seen. It has a slight blood supply, which is not apparent in this magnification. The joint capsule is still not formed. D same fetus. Note the separate iliac and pubic components of the acetabulum.

rounded by fibrous perichondrium, which supplies a few invading blood vessels to its substance

SPECIMEN 4 (fetus aged about 20 weeks) —In sections of the hip joint through the sacroiliac joint, the center of ossification of the ilium had expanded in all directions so that about three fourths of it was ossified. The sacroiliac joint space was wider and better developed than in the specimens previously described. The ilium was surrounded by fibrous periosteum in which considerable new bone formation was apparent, and this periosteum was extremely vascular, supplying the bone with new blood vessels. The acetabulum, head, neck and trochanter were composed of cartilage, but a small center of ossification appeared in the posterior superior, or iliac, portion of the acetabulum. The acetabulum was surrounded on its nonarticular surface by thick fibrous perichondrium, and this was continuous at the rims of the acetabulum with well formed cotyloid ligaments. The blood supply of the acetabulum was extremely profuse, and several vessels entered its substance from all regions of the periphery. The capsule of the hip joint could be identified as thin strands of wavy fibers originating from the acetabular edges and inserting into the superior and inferior portions of the femoral neck. (We have not attempted to reconstruct anatomically the blood supply of the head and neck, but it is obviously derived from vessels which enter by way of the capsule near its insertion into the neck.) In this specimen, blood vessels entered on both the upper and the under surface of the neck and appeared to anastomose freely. The head was surrounded by a few rows of flattened cartilage cells. It was possible to determine that the head was moderately vascular, the vascular spaces in general being away from the convex area. The ligamentum teres and the fovea centralis were recognized, and both these and the area of insertion of the ligament were vascular. The cotyloid ligaments were well formed.

The 20 week fetus showed the following developmental changes from the appearance of the 14 week embryo. The cartilages of the acetabulum were surrounded by a vascular rim of perichondrium. The femoral head was more shapely and extremely vascular. There were a well defined neck and trochanter and a beginning joint capsule. The concavity of the acetabulum opposite the foveal portion of the head showed a vascular layer which represented the site of emergence of the ligamentum teres. The head, as has been mentioned, was composed of hyaline cartilage with a peripheral rim of flattened cartilage cells, and at its junction with the neck it was covered with a layer of vascular connective tissue which undoubtedly represented primitive synovium. The trochanter seemed to receive an independent blood supply from the muscles of its lateral aspect and also received some blood supply from blood vessels of the capsule. The impression received was that the majority of the blood vessels supplied the head and trochanter and that the neck of the femur derived a less profuse blood supply from an anastomotic cross circulation. The capsule was even and delicate and was continuous with the perichondrial tissues surrounding the acetabulum. In one section the femoral head and neck, trochanter and ligamentum teres were noted. The ligamentum teres was liberally supplied by blood vessels which were linked up with those of the fovea centralis, but these blood vessels did not seem to penetrate the cartilage of the femoral head. The blood vessels in the ligamentum teres could be traced to a plexus in the acetabulum. There were some zones of slight calcification of the cartilage of the femoral head in the areas related to the most protuse blood supply, ossification was not seen.

Summary—The 20 week embryo shows the structures of the hip joint in a fairly mature state. The shape of the head, neck and trochanter is similar to that of these structures in the infant. The capsule

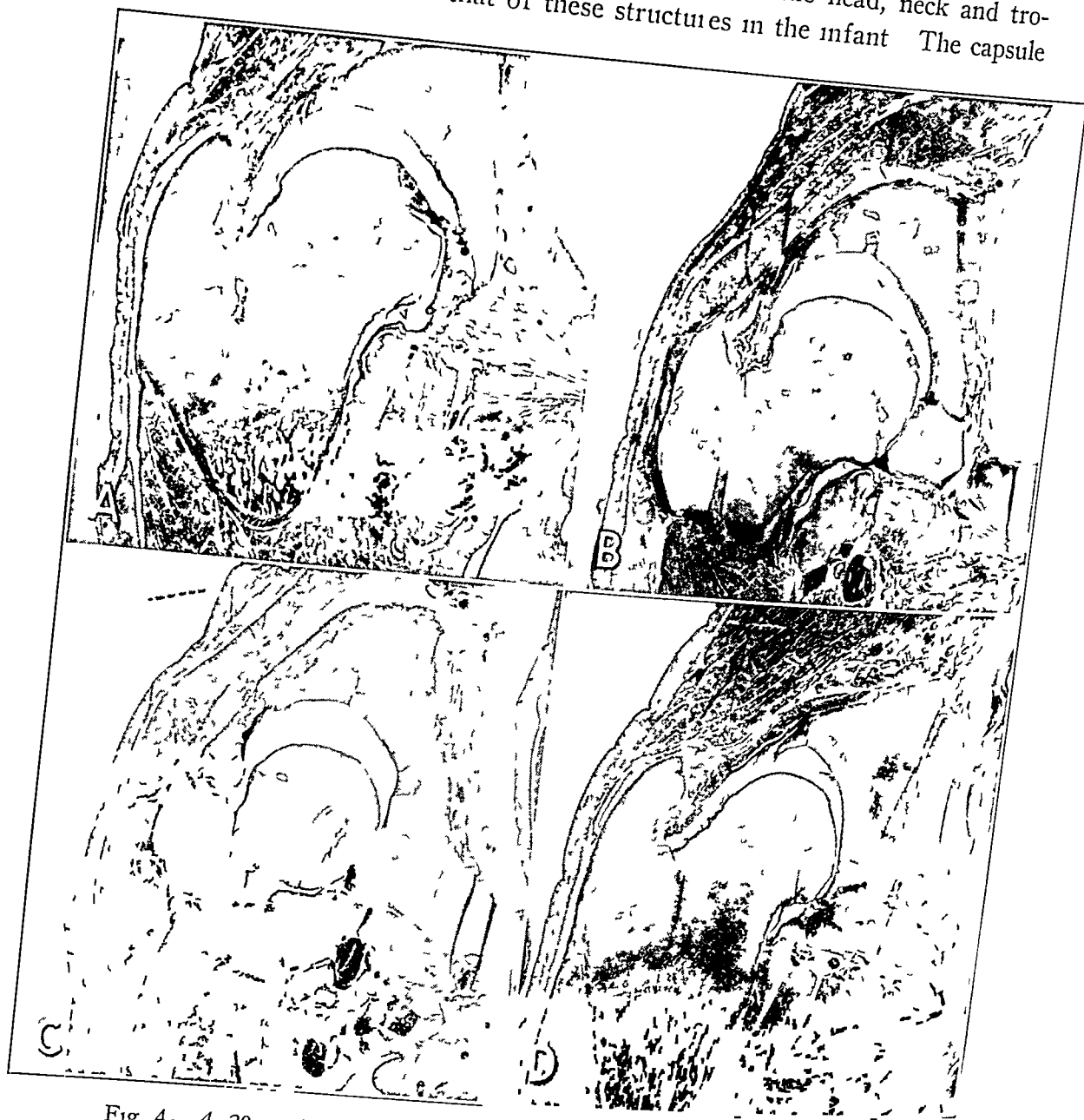


Fig 4—A, 20 week fetus, showing the head, neck and trochanter of the femur and the acetabulum. Notice the profuse blood supply of all the cartilages. The ligamentum teres is seen and also contains a profuse blood supply. The capsule may be seen for the first time, inserting into the notch between the neck and the trochanter. There is a vascular membrane covering the surface of the upper end of the neck, this represents the primitive synovium, not readily seen in the low magnification. B, same fetus, showing the same complete acetabulum. C, same fetus. Notice that the hip joint is at the level of the pubic symphysis. D, same fetus, showing the center of ossification in the acetabulum.

of the hip joint can be identified for the first time. The capsule brings with it a profuse blood supply, which enters the head at its junction with the neck on both its superior and its inferior surface. These vessels penetrate the head in various directions, tending to converge near the convex portion. Small zones of calcification of the cartilage are identified, but true ossification does not appear until later. The first center of ossification seems to develop in the acetabulum—in its posterior superior portion, the iliac portion. The cavity of the acetabulum, the ligamentum teres and the fovea centralis are rich in blood vessels, but these blood vessels do not seem to penetrate into the femoral

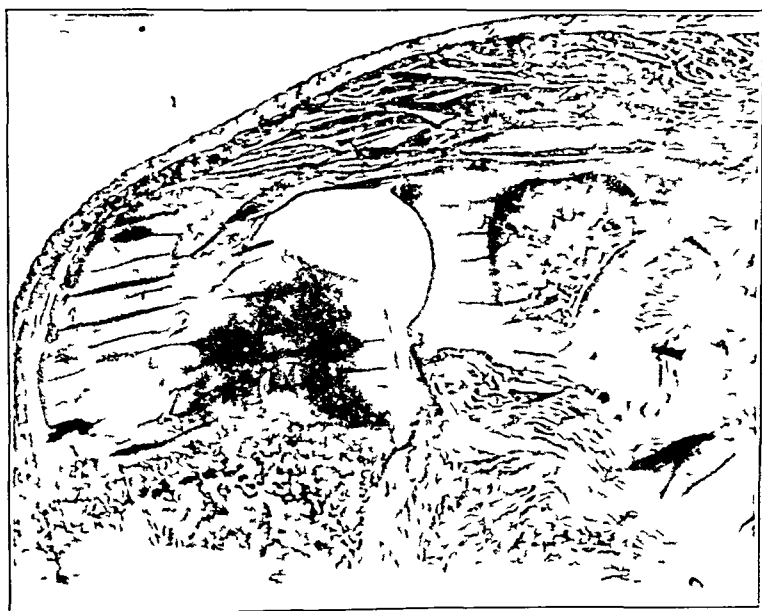


Fig 5—Fetus of 30 weeks. There are no striking changes from the appearance described for the 20 week fetus, but the structures are larger. The center of ossification in the acetabulum is somewhat larger. Some of the head is missing

head. A structure identifiable as primitive synovium makes its appearance simultaneously in the acetabulum surrounding the insertion of the ligamentum teres and in the upper and under surfaces of the neck at the reflection of the joint capsule.

SPECIMEN 5 (fetus aged about 25 weeks)—The structures entering into the formation of the hip joint were slightly larger than in the fetus previously described. The femoral head and neck and the greater trochanter were all present in cartilages, and over the superior and inferior aspects of the neck the vascularity of the primitive synovium was more apparent than in specimen 4. The ligamentum teres and the fovea centralis were better developed. The femoral head appeared to lie somewhat anterior to a plane through the center of the acetabulum and to

suggest a certain degree of torsion of the neck of the femur. In other respects the appearance did not differ appreciably from that of specimen 4.

SPECIMEN 6 (fetus aged about 30 weeks) —The femoral head and neck and the trochanter were all present as cartilage, with a primitive epiphysial line fairly well down the shaft (about the level of the lesser trochanter). The acetabulum possessed a well formed center of ossification, but it was extremely shallow. The cartilages of the head and trochanter were more definitely formed, and some of the blood vessels extended down to the epiphysial line, where they probably anastomosed with the nutrient artery. The primitive synovium of the femoral neck was even more vascular than that previously seen. The neck was short and stubby, and the greater trochanter appeared to extend upward to about the level of the top of the femoral head, giving the neck a coxa vera attitude. The joint capsule, while better developed than in the specimens previously described, was not a thick, fibrous structure. In other respects there were no striking differences from the 25 week fetus.

GENERAL SUMMARY

A preliminary review of the embryology of the hip joint studied by means of horizontal serial sections through the embryo or fetus has been made on a series of specimens, normal embryos and fetuses 6, 10, 14, 20, 25 and 30 weeks old being used.

In the 6 week embryo the cartilages of the ilium and femur are formless structures, and only a suggestion of the joint space exists.

In the 10 week embryo the iliac cartilage is well formed, as is the acetabular cavity, but the femoral head is club shaped and not well differentiated. The cotyloid ligament and the ligamentum teres are present, but no definite capsule is developed, and there is no vascularization of the cartilaginous structures.

In the 14 week fetus the shape of the femoral head and that of the acetabulum more closely resemble the shape of these structures in the infant. The cartilages show beginning vascularization, although the capsule still remains unidentified.

In the 20 week fetus the acetabulum begins to ossify, and ossification proceeds rapidly throughout the remainder of intrauterine life. The capsule is present and is vascular. The blood supply of the femoral head and neck and of the trochanter may in part be traced to blood vessels entering by way of the capsule. The trochanter receives an additional blood supply from the lateral muscles. The ligamentum teres can be noted, and the synovium appears in the acetabulum and around the neck of the femur. It becomes increasingly vascular in the older fetuses.

In fetuses up to 30 weeks the enlargement of the capsule and the increase in its vascularity have been traced. A certain amount of remolding of the femoral head and neck, so that they resemble these structures in the infant, has been described.

TEXTBOOK OF PHYSIOLOGY OF THE HUMAN BODY AND OF THE HUMAN MIND

PERIPHERAL DISTRIBUTION OF SENSORY AND MOTOR FIBERS AND ANATOMICAL RELATIONS OF THE SPINAL NERVES AND MUSCLES INVOLVED

WILLIAM S. JENNINGS AND
THEODORE W. SWANN

The work of the physiologists Gaskell¹ reported in 1886 on the distribution of afferent nerve impulses initiated by the viscera later received clinical interpretation by Ross. Many observers contributed to its further development among whom Head,² Mackenzie,³ Morley,⁴ and Lennander⁵ may be mentioned. Cutaneous areas were mapped out by a study of cutaneous superficial hyperaesthesia, the distribution of the rash along the course of nerves in cases of herpes zoster, and the direction of the subjective symptom referred pain. To Head is due the credit for mapping out the distribution of the afferent somatic nerve in cases of structural and functional changes in the pelvis of the kidney and the ureter. This accumulation of clinical data, however, has been based essentially on the zoning out of cutaneous areas by actual tactile approach without complete consideration of the anatomic structure involved.

Though all this accumulated knowledge is based mainly on clinical and physiologic observations, the anatomists have been prone to accept it. The cutaneous and muscular response to visceral disturbance is based on a reflex, the intricate course of which is at present beyond actual physical demonstration. This point of view was clearly expressed by Gaskell as follows:

1 Gaskell, W. H. On the Structure, Distribution and Function of the Nerves Which Innervate the Visceral and Vascular System, J. Physiol. 44, 1886.

2 Ross, J. On the Segmental Distribution of Sensory Disorders, Brain 10 333, 1888.

3 Head, H. A Disturbance of Sensation with Especial Reference to the Pain of Visceral Disease, Brain 1641, 1894.

4 Mackenzie, J. Contribution to the Study of Visceral Symptoms Associated with Visceral Disease, M. Chron. 161-94, 1899. Symptoms and Their Interpretation, London, Shaw & Sons, 1909.

5 Morley, J. Abdominal Pain, New York, William Wood & Company, 1914.

6 Lennander, K. G. Observations on the Sensibility of the Abdominal Cavity, translated by A. J. Baker, London, John Bale, Son & Daniel, n. d. 1903.

It is hopeless at present to follow any nerve or group of nerve-fibres through a mass of ganglion cells with which it is in connection, it is impossible by simple anatomical investigation to trace these nerve-fibres further, the course of a nerve's fibre can however be traced by its physiological action as well as by its histological characters

The knowledge accumulated by the various observations and interpretations has laid down a foundation for these concepts. Further advance, however, must be made mainly on the basis of anatomic investigation aided by clinical and experimental support

In this work, instead of the customary tactile method, the modus operandi chosen was elicitation of deep hyperalgesia by deep pressure on or in the vicinity of nerves or nerve fibers, such as is noted over McBurney's point in cases of acute appendicitis. In addition, one palpates for muscle spasm

The recognition in cases of calculus of the ureter of a constant point of maximum tenderness, located about 1 inch (2.5 cm) medial to the anterior superior spine of the ilium and a little above the inguinal (Poupart's) ligament, led me not only into further urologic studies but into studies in the anatomic laboratory.⁷ This collateral study included the various muscles, nerves and arteries of the abdominal and related regions. It was hoped further to correlate the growing clinical knowledge with the corresponding anatomic observations, concerning which the standard textbooks of anatomy proved inadequate

ANATOMIC RELATIONS

That a clearer grasp may be obtained of the intricate involvement of certain anatomic structures in the production of the ureteral reflex, this section on the anatomic relations is presented. Consideration will be given to the following structures: the branches of the lumbar plexus, such as the iliohypogastric, ilioinguinal and genitofemoral nerves, particularly their origin, course and distribution, the obliquus externus and internus and transversus and rectus abdominis muscles, and branches of the iliac and femoral arteries, especially the deep circumflex iliac artery

The relations of these structures to each other and to the associated viscera will be included

The truncal muscles may be divided into four groups, as follows

- 1 The dorsal axial muscles—the posterior group involving the body, spinous and transverse processes of the vertebrae and ribs
- 2 The posterior muscles of the abdominal wall and pelvis—the psoas, iliacus and quadratus lumborum

⁷ I was permitted to study the students' dissections at the Long Island College of Medicine and also adjunct and independent dissection

3 The lateral muscles of the abdominal wall—the obliquus externus, obliquus internus and transversus abdominis

4 The anterior muscles of the abdominal wall—the rectus abdominis and the pyramidalis

The longitudinal muscles are connected by means of an intercommunicating group of muscles, in the thorax by the intercostal muscles and in the abdomen by the obliquus and transversus muscles. These three groups of muscles (posterior, lateral and anterior) are innervated by spinal nerves arranged on an obviously segmental basis, as described by Head, and containing sensory, motor and sympathetic fibers. Cunningham⁸ stated that there is fusion of the segmental myotomes in the longitudinal posterior muscles, which are supplied by a series of muscular branches derived from the posterior rami of contiguous nerves.

It is apparent that the association of the longitudinal and intercommunicating muscles may be of help in distributing nerve fibers in a perpendicular direction beyond the more or less segmental direction of the nerves derived from the cerebrospinal nervous system.

This is further aided by the anastomosis and plexus formation in the obliquus internus muscle of individual branches of the lower intercostal nerves, the branches of the first lumbar nerve and whatever nerve filaments are carried by the deep circumflex iliac artery in its course upward.

Nerves—The first lumbar nerve is a motor and sensory nerve, emerging from the intervertebral foramen, which sometimes (in 50 per cent of cases) receives a small branch from the twelfth dorsal nerve. It also has a relation to the sympathetic nervous system, by way of the gray rami communicantes, receiving branches from one or two sympathetic ganglions (frequently one ganglion sends branches to two nerves). The white rami communicantes, either independently or incorporated with the corresponding gray rami, join the upper part of the lumbar region of the sympathetic trunk. The first lumbar nerve then divides in the substance of the psoas muscle into an iliohypogastric and an ilioinguinal nerve, the iliohypogastric lying above and the ilioinguinal below. Two independent roots from the first and second lumbar nerves unite to form a slender trunk, the genitofemoral nerve.

In their composition, course and distribution these nerves resemble closely the lower thoracic nerves, with which they are in series. Many authors classify the first lumbar nerve as the thirteenth dorsal nerve because of this similarity.

⁸ Cunningham D. J. Text-Book of Anatomy, ed. 5, edited by A. Robinson, New York, William Wood & Company, 1928.

Iliohypogastric Nerve There are varying opinions regarding the origin of this nerve,⁹ but Bardeen and Elting¹⁰ claimed to have found it originating from the first lumbar nerve in 183 of 246 instances, which is the largest series reported, from the twelfth dorsal nerve in 63 of 246 dissections, and from the eleventh dorsal nerve in rare instances (1 case)

The iliohypogastric nerve rests on the quadratus lumborum muscle and behind the kidney, not far from the inferior pole. It pierces the fascia and lies between the transversus abdominis and the obliquus internus muscle, hugging mainly the latter. In this location the nerve frequently spreads out over a wide area, and a free anastomosis and plexus formation exist. In 8 instances, I have observed an anastomosis with the eleventh dorsal nerve twice, with the twelfth dorsal nerve five times and with the ilioinguinal nerve three times. Cruveilhier has also observed frequent anastomosis with the twelfth dorsal nerve. In 12 dissections the iliohypogastric nerve was found five times within the iliac fossa.

When the internal oblique muscle was folded over, it was observed that the deep circumflex iliac artery arises from the lateral side of the external iliac artery and occasionally from the femoral artery, immediately above the inguinal ligament. Its course is above the lower border of this ligament, enclosed in a fibrous canal formed by the union of the fasciae of the transversalis and the iliac muscle. It runs laterally and upward to the anterior superior spine of the ilium. A little beyond this it pierces the transversus abdominis muscle and is continued between the transversus and the obliquus internus muscle. Two branches are given off: (1) a muscular branch, which ascends vertically to the muscles of the abdominal wall to anastomose with the lumbar and epigastric arteries, and (2) cutaneous branches, piercing the muscles and terminating in the skin over the crest of the ilium to anastomose with other vessels.

The deep circumflex iliac artery, the iliohypogastric nerve, occasionally the ilioinguinal nerve and in rare instances the twelfth dorsal nerve travel obliquely in the same plane, but in opposite directions. They frequently cross. There is an intricate and varying interinvolvement of these structures, which is summarized in table 1. I have seen an extensive plexus of nerves forming loops, networks and rings over a wide area embracing the lower four intercostal nerves, some fibers

9 Hovelacque, A. *Anatomie des nerfs crâniens et rachidiens et du système grand sympathique, chez l'homme*, Paris, Gaston Doin & Cie, 1927.

10 Bardeen, C. R., and Elting, A. W. *A Statistical Study of the Variations in the Formation and Position of the Lumbo-Sacral Plexus in Man*, *Anat. Rec.* 19: 124, 1901. Bardeen, C. R. *A Statistical Study of the Abdominal and Pelvic Nerves in Man*, *Am. J. Anat.* 1: 203, 1901-1902.

of which terminate within the plexus, others form a loop to recommunicate with each other and still others anastomose with their own or other branches, terminate in the deep circumflex iliac artery or

TABLE 1—*Relation of Lower Spinal Nerves to Deep Circumflex Iliac Artery (18 Dissections)*

	Number of Instance	Crossing of Deep Circumflex Iliac Artery by Nerve					
		Main Trunk Number of Instances		Muscular Branch Number of Instances		Cutaneous Branches Number of Instances	
		Anteriorly	Posteriorly	Anteriorly	Posteriorly	Anteriorly	Posteriorly
Iliohypogastric nerve	10	3	1	7	8	9	5
Ilioinguinal nerve	7						
Twelfth dorsal nerve	3						
Total	21						
Summary A	10	One spinal nerve crossed artery					
		Two spinal nerves crossed artery					
	1	Three spinal nerves crossed artery					
Summary B		Spinal nerves passed anterior to artery					
	3	Spinal nerves passed posterior to artery					
	2	Spinal nerves passed anterior then posterior, to branches of artery					
	3	Spinal nerves passed posterior then anterior to branches of artery					
Branch of iliohypogastric nerve	4	Terminated in deep circumflex iliac artery					
Branch of iliohypogastric nerve	2	Coursed parallel to main trunk of deep circumflex iliac artery					
Formation of nerve plexus	7	Involved deep circumflex iliac artery					

TABLE 2—*Relation of Point of Emergence* of the Iliohypogastric Nerve from the Internal Oblique Muscle to the Anterior Superior Spine of the Ilium (23 Dissections)*

Inches	Mesial to the Anterior Superior Spine		Inferior to the Anterior Superior Spine	
	Number of Instances	Percentage of Cases	Number of Instances	Percentage of Cases
0.5	2	8.7	2	8.7
1.0	14	60.9	3	13.0
1.5	4	17.4	2	8.7
2.0	3	13.0	1	4.4
On level with anterior superior spine			15	65.2
Total	23	100.0	23	100.0

* This point corresponds to the point of maximum tenderness

continue as a branch running along the course of the artery. All of these fibers come into direct contact with the deep circumflex iliac artery.

The point of emergence of the iliohypogastric nerve from the obliquus internus muscle varies in relation to the anterior superior spine of the ilium (table 2)

The iliohypogastric nerve becomes cutaneous 15 inches (38 cm) above the subcutaneous inguinal ring. The branches of the iliohypogastric nerve are: 1. A muscular branch to the muscles of the abdominal wall, including a branch to the pyramidalis muscle, which is also supplied by a branch of the twelfth dorsal nerve. Sometimes a branch is given off to the rectus abdominis muscle (in 2 of 5 cases, according to Ruge, in 14 of 112 cases according to Bardeen). Eisler followed the nerve filaments to the great tendinous insertion of the rectus muscle.

2. A lateral cutaneous branch (similar to that of an intercostal nerve) to the lateral side of the buttock.

3. An anterior cutaneous branch to the skin of the anterior abdominal wall, below the level of the last thoracic nerve and above the os pubis.

Anastomosis. The branches to the internal oblique muscle on its deep surface anastomose with the filaments coming from the last four intercostal nerves, forming a veritable plexus (Hovelacque).

Ilioinguinal Nerve. This nerve is the second branch given off from the first lumbar nerve. It may also receive fibers from the last thoracic nerve. Not infrequently the iliohypogastric and the ilioinguinal nerve are represented for a longer or shorter part of their course by a single trunk. When separate, the nerve takes a course similar to that of the iliohypogastric nerve, but at a lower level, as far as the anterior abdominal wall. The ilioinguinal nerve was missing in 26 of 100 plexuses examined by Severeano. There is a variation in origin. The nerve was observed by Bardeen and Elting to arise from the first lumbar nerve in 229 of 246 instances. Ancel and Sencert made the same observation in 63 of 64 instances. The nerve has also been observed to arise from the twelfth dorsal nerve only or to receive at the same time a branch from the first lumbar nerve (in 113 cases by Bardeen and Elting).

The caliber of the ilioinguinal nerve is generally 1 to 1.5 mm, that of the iliohypogastric nerve is at least 2 mm. The abdominal branch is very short, and not exceptionally loses itself in the large muscles of the anterior abdominal wall. I have also observed (in 7 of 11 instances) that it anastomosed frequently with the twelfth dorsal nerve, the iliohypogastric nerve and the ilioinguinal nerve and engaged itself in plexus formation and looping. Most frequently it was observed to go to the scrotum (6 instances) and occasionally to the pubis (2 instances). It was also seen to unite with the iliohypogastric nerve (5 of 11 instances). Occasionally the ilioinguinal nerve is very small and ends by joining the iliohypogastric nerve, when this occurs, a branch from the iliohypogastric nerve takes the place of the ilioinguinal nerve, or the ilioinguinal nerve may be absent (Gray¹¹).

¹¹ Gray, H. *Anatomy, Descriptive and Applied*, ed. 18. Philadelphia: Lea & Febiger, 1910.

Course The nerve lies between the transversus and the obliquus internus muscle and pierces the obliquus internus farther forward and lower than does the iliohypogastric nerve, it distributes branches to this muscle and accompanies the spermatic cord through the subcutaneous inguinal ring

Branches The ilioinguinal nerve distributes cutaneous branches to (1) the anterior abdominal wall over the symphysis pubis, (2) the thigh over the proximal and medial parts of the femoral triangle and (3) the superior part of the scrotum and the root and dorsum of the penis (of the mons veneris and the labium majus in the female)

The branches last mentioned are contiguous to branches of the perineal and pudendal nerves. As to the genital branch, it is not rare to see it fuse with the genital branch of the iliohypogastric nerve (Hovelacque). The ilioinguinal nerve possesses no perforating branches.

Genitofemoral Nerve ^s This nerve arises from the first and second lumbar nerves and unites in the substance of the psoas major muscle to form a slender trunk. It appears on the posterior abdominal wall, lying on the psoas major muscle and extending downward on the lateral aspect of the common and external iliac vessels and behind the ureter to the inguinal ligament. At a variable point above that ligament it divides into two branches, as follows

1 The external spermatic branch (small nerve) crosses the termination of the external iliac vessels and, together with the ductus deferens and the testicular and external spermatic vessels, enters the inguinal canal through the abdominal inguinal ring. It terminates by supplying small branches to the skin of the scrotum and the adjacent part of the thigh. In the female it accompanies the round ligament to the labium majus. During its course it gives off small branches to (1) the external iliac artery and (2) the cremaster muscle and communicates with (3) the spermatic plexus of the sympathetic nerve.

2 The lumboinguinal branch extends to the thigh, lying on the lateral aspect of the femoral artery. It becomes cutaneous by passing through the fossa ovalis or through the iliac portion of the fascia lata and supplies an area of skin over the femoral triangle lateral to that supplied by the ilioinguinal nerve. It communicates in the thigh with a branch of the femoral nerve and gives off minute branches to the femoral artery.

Muscles—**Obliquus Externus Abdominis Muscle** This muscle, being voluminous, has been termed by the French the *grand oblique*. It is musculoaponeurotic, the lateral part being muscular and the ventral part aponeurotic. Its origin is muscular and it terminates in an aponeurosis on a level with the ninth costal cartilage and the anterior superior spine of the ilium. I found that the distance between this muscular edge and the lateral margin of the rectus muscle varied as

follows no space, 1 instance, 2.5 cm, 5 instances, and 3.75 cm, 2 instances. In 5 of 8 instances, therefore, there is 1 inch (2.5 cm) space. The lower muscular edge was seen to be above the anterior superior spine in 7 of 10 instances and below it in 2 instances. These measurements were taken at the level of the twelfth rib.

Obliquus Internus Abdominis Muscle. This is a broad, thin sheet of muscle which lies between the external oblique and the transversus muscle. I noted that its muscular part extended to the lateral edge of the rectus muscle in 11 of 13 instances and 1.25 cm lateral to the edge of the rectus muscle in the remaining 2 instances. This muscle is apparently not responsible for the fascial space previously described.

Transversus Abdominis Muscle. This muscle terminates in an aponeurosis, which is widest at the level of the interval between the last rib and the iliac crest. The following variations in the extent of this interval were observed in 9 instances: (1) up to the edge of the rectus muscle, in 1 instance, (2) 2.5 cm lateral to the edge of the rectus muscle, in 7 instances, and (3) 3.75 cm lateral, in 1 instance.

In summarizing this small series, it was observed that there was a striking similarity between the aponeurotic interval of the obliquus externus and that of the transversus abdominis muscle.

ZONES

The anatomic data previously presented require clinical application to be of practical value.

In the muscles of group 1 (the dorsal axial muscles) elicitation of the well known Murphy sign¹² may depend apparently on deep hyperalgesia of the area over these muscles, which are supplied by the posterior rami of the regional spinal nerves. Costovertebral tenderness depends, I believe, on pressure over the twelfth dorsal nerve, which enters into the formation of the first lumbar nerve. From investigations now in progress, I believe that the first lumbar nerve is more concerned in the production of this hyperalgesia than is the twelfth dorsal nerve.

I am of the opinion that there is spasm and perhaps hyperalgesia of the muscles of group 2, which consist of the psoas, the iliacus and the quadratus lumborum muscle. I have been unable to find any reference to such hyperalgesia in the literature.

Groups 3 and 4 are the two groups of muscles described in this paper. Group 3 consists of the lateral muscles of the abdominal wall, the obliquus externus and internus and the transversus abdominis, and group 4 consists of the anterior muscles, the rectus abdominis and the pyramidalis. In this study two methods were used for palpation of the abdomen. Muscular spasm and muscular tenderness were elicited by

¹² Murphy, J. B. *Murphy's Surgical Clinics*, Philadelphia: W. B. Saunders Company, 1912, vol. 1, p. 459.

a moderate diffuse pressure with the flat of the hand, for deep hyperalgesia more localized pressure with the finger was used. These muscular signs are generally pronounced in the posterior group, moderate in the lateral group and mild in the rectus muscles of the abdominal wall. With the patient prone, the fleshy fibers of the obliquus externus muscles, if in spasm, can be palpated as a distinct edge. This edge is located about 1 inch (2.5 cm) lateral to the margin of the rectus abdominis muscle. Normal variations of muscular development modify this finding. The depression between the obliquus externus and the rectus muscle is termed the fascial space.

The spasm and tenderness of the external oblique muscle varies in different parts, being most pronounced above the crest of the ilium, where its nerve supply is abundant, and least marked or absent at the upper part of the muscle. In contrast, the hyposensitive fascial space separates the mildly tender edge of the rectus muscle from the more tender fleshy edge of the external oblique muscle. Tenderness is usually greatest along the fleshy edge of the external oblique muscle. The rectus muscle also possesses a varying degree of muscle spasm and tenderness. For convenience, this muscle has been divided into a medial and a lateral edge and a body. As a rule there are slight tenderness of the medial edge, moderate tenderness of the lateral edge and more marked tenderness of the intervening body. This variation is dependent, I believe, on the nerve supply. The intercostal nerves pierce the deep surface of the rectus muscle and spread out close to the lateral edge. The nerves extend to adjoining segmental areas of the rectus muscle and emerge to become cutaneous. This accounts for the inequality of tenderness in this muscle.

The rectus abdominis, like the external oblique, muscle manifests the greatest amount of spasm and tenderness in its lowermost parts. The upper limits of hyperalgesia may extend as high as the eighth or ninth dorsal nerve, and occasionally higher (the umbilicus corresponds to the tenth dorsal nerve).

Deep hyperalgesia has been observed to correspond with the course, distribution and emergence of the nerves and nerve fibers involved in the reflex.

I have observed five points of deep hyperalgesia, including the point of maximum tenderness. These were

1. A point at the level of the first lumbar nerve, lateral to the spines of the vertebrae.

2. The posterior part of the peak of the crest of the ilium. This corresponds, I believe, to the course of the first lumbar nerve within or above the hollow of the iliac fossa and its emergence through the transversus muscle.

3 The point of maximum tenderness, which is located about 1 inch (2.5 cm) medial to and on a level with the anterior superior spine of the ilium¹³ Variations will correspond with the data in table 2 Tenderness at this point, I believe, is produced by the emergence of the iliohypogastric nerve from the internal oblique muscle There is also a less clearly defined area of tenderness around this point, about the size of a half-dollar This, I believe, corresponds to formation of a plexus containing the twelfth dorsal or first lumbar nerve

4 A point directly above and lateral to the crest of the pubis Tenderness at this point is apparently due to the termination of a branch of the first lumbar or twelfth dorsal nerve

5 Within the femoral (Scarpa's) triangle, along the femoral sheath This corresponds, I believe, to the point of emergence of the genitofemoral nerve and other fibers of the first lumbar nerve This point has been described by Livingston,¹⁴ who elicited tenderness in this region by pinching the skin

In this study the reflex has been followed to the femoral triangle In the lower extremity these points have not been worked out in detail, but in general it may be stated that other points of tenderness have frequently been found along the inner part of the thigh, in the popliteal space, in the inner part of the calf and in the knee and ankle, particularly in the mesial rather than in the lateral aspect

In addition, a belt of hyperalgesia, tapering to about 2 inches (5 cm) and corresponding to the twelfth dorsal and first lumbar nerves, which connect all the points of tenderness previously mentioned, radiates over the crest of the ilium, above the inguinal ligament, to the pubis and to the femoral triangle and then along the course previously mentioned

I have observed patients who complained of pains in the hip, knee and ankle joints during and after an attack of calculus of the ureter, which either improved or disappeared after the attack had subsided I am of the opinion that such symptoms are not truly arthritic, but are manifestations of nerve irritation in the region of these joints

All of the previously mentioned findings have been observed to be bilateral, with variations in frequency depending on the underlying pathologic condition Even in the presence of a unilateral lesion a milder contralateral reflex was observed This will be considered later in more detail

13 After completion of this work, description of a somewhat similar point was found in the literature (Barney, J. D. A Point in the Clinical Diagnosis of Ureteral Calculus. A Preliminary Report, *Ann Surg* 107:636 [April] 1937)

14 Livingston, E. M. A Clinical Study of the Abdominal Cavity and Peritoneum, New York, Paul B. Hoeber, Inc., 1932, pp. 633-634

These studies have been made on patients presenting signs referable to the abdominal wall analogous to those associated with chronic or subacute intra-abdominal conditions rather than with the tense muscles of the "acute abdomen"

The expression "Tenderness is found along the course of the ureter" is explicable by what is known as vertical continuation downward of Tournier's point¹⁵ It is my opinion that this vertical line of tenderness corresponds to the deep hyperalgesia observed at or about the lateral margin of the rectus abdominis muscle

In ureteral disturbances, pain and hyperalgesia have frequently been found to be limited to either the right or the left side In intraperitoneal conditions, however, such demarcation is not so evident

TABLE 3—Analysis of One Hundred Cases in Which Routine Cystoscopic Examination Was Done for Suspected Urologic Conditions

Group 1 Definite Diagnosis		Group 2 Presumptive Diagnosis		Group 3 No Diagnosis of Renal or Ureteral Disease	
	No of Cases		No of Cases		No of Cases
Calculus	17	Obstruction of ureter	12	Hematuria	12
Ureter	12	Hydronephrosis	9	No diagnosis	3
Pelvis	3	Ptoxis	3	Pathologic condition of bladder	7
Kidney	2	Pyelitis of pregnancy	3	No findings	3
		Tumor of kidney	4	No diagnosis with posi- tive findings	12
		Pathologic condition of bladder	0		
		Tuberculous pyelonephrosis	1		
		Retroperitoneal abscess	1		
		Infarct of kidney	1		
		Spasm of ureter	2		
		Scoliosis	1		
Total	17		46		37

ANALYSIS OF ONE HUNDRED CASES (TABLE 3)

This report is based on 100 cases in which routine cystoscopic examination was made at the Cumberland Hospital under the direction of Dr John E Jennings, director of surgery, and Dr R E Kinloch, attending urologist, and at the Israel-Zion Hospital under the direction of Dr William Linder, chief of surgery, and Dr Abraham Hyman Several of my private cases were included in the study

The examinations were performed by the urologists of the service and consisted of the usual routine including intravenous and retrograde pyelographic examination and roentgen and laboratory examinations Many of the patients were operated on I was present at each cystoscopic examination, and the hospital records have been transcribed to my personal notes, for the sake of completeness

¹⁵ Piersol, G M Piersol's Human Anatomy Including Structure and Development and Practical Considerations edited by G C Huber ed 9 Philadelphia, I B Lippincott Company 1930 pp 1898 1901

In 14 of the 17 cases in group 1, which consists entirely of cases of calculus, the diagnoses were made by the points and areas of hyperalgesia previously enumerated and they coincided with the final diagnoses, which were made by urologic methods. The calculi in these cases were located as follows: on the right side, in 9, on the left, in 7, and bilaterally in 1 case. The cases may be further subdivided into those in which the calculus occurred in the ureter (12 cases), in the pelvis of the kidney (3 cases) and in the kidney (2 cases).

Analysis of table 3 reveals that in group 2, or the cases in which no calculus was present, the tender points and areas indicated the involvement in 71.8 per cent of the cases, as proved by urologic methods of diagnosis. In the cases of hematuria in group 3 the difficulty in arriving at a diagnosis makes further comment inadequate. It may be mentioned, however, that mild hyperalgesia was frequently elicited, which coincided with other clinical findings. The conclusions were suggestive, but not definite.

Group 3, in which no definite diagnosis was established, will not be considered here, except to say that the cases in which the findings were not significant served as ideal controls. In the group in which the diagnosis was presumptive the following case will show the difficulty in establishing an accurate diagnosis.

The patient in case 9, a woman, was admitted to the orthopedic service at the Israel-Zion Hospital on Dec. 27, 1933, having been admitted to the same service on three previous occasions for treatment of scoliosis, relief of which was attempted by the application of plaster jackets. An appendectomy was performed in 1923 and a right salpingectomy for an ectopic pregnancy in 1929. The patient complained of burning on urination, frequency of voiding, nocturia, stoppage of urinary flow and pain extending posteriorly on the left side over the lumbar region and radiating to the vulva and the thigh. Urologic examination revealed a slight spasm of the left ureter, and roentgen examination showed that the twelfth dorsal vertebra was wedge shaped, with a sharp angulation to the left and a corrugated left border.

Campbell¹⁶ stated that "in spinal caries pressure on the nerve trunk produces pain at the periphery and also caries of the upper lumbar vertebrae may be mistaken for renal calculus (Woolsey)."

BILATERALITY

In cases in which the lesion is apparently unilateral, pain is frequently bilateral. This phenomenon has been termed "the renorenal reflex." Two theories have been advanced to explain it. One group of observers has contended that there is actually a bilateral pathologic condition, though on only one side is it actually demonstrable, another

¹⁶ Campbell, W. F. *Surgical Anatomy*, Philadelphia, W. B. Saunders Company, 1921.

group has contended that there is a unilateral pathologic condition which produces a contralateral reflex. The physical basis for these assumptions has been arrived at subjectively, for the most part.

In my analysis, based on 100 cases, this problem has been approached from the objective point of view, on the basis of deep hyperalgesic zones rather than of pain per se. In group 1, 17 cases of proved unilateral calculus were reviewed. Although this group of cases is small, the observations were carefully made and were supported by data in other cases not recorded here. Bilateral signs were observed in 5 of these 17 cases, or 29.4 per cent (table 4). As the investigation of the reflex becomes more detailed, the percentage should be higher.

In reviewing this group it is noted that the percentage of instances in which there was a bilateral reflex varies from 8.3, in the cases of undiagnosed hematuria, to 29.4 in the cases of calculus of the ureter. On comparison of these two extremes it is obvious that the intensity of the impulse may play the important role. In cases of hematuria the reflex

TABLE 4—*Bilaterality of the Renorenal Reflex*

Group	Lesion	No. of Cases	Bilateral Reflex	Percentage
1	Calculus	17	5	29.4
2	Ptosis	3	1	33.3
	Hydronephrosis	9	3	33.3
	Obstruction of ureter	12	3	25.0
	Pyelitis	3	1	33.3
3	Hematuria	12	1	8.3

is mild, whereas in cases of calculus it is pronounced. The variation apparently depends on the underlying pathologic condition. Patients with ptosis, hydronephrosis, pyelitis or calculus possess the contralateral reflex in approximately the same percentage, whereas for patients with obstruction of the ureter the incidence is less and for patients with the hematuria the least. In conclusion, it may be stated that the greater the hyperalgesia, the more frequently the contralateral reflex appears. Pottenger¹⁷ mentioned that the strength of the nerve impulse is sufficient to overcome the threshold of resistance.

Head also concluded that there is a tendency for both pain and tenderness to appear on the opposite side at the same spinal level.

PARAVERTEBRAL INJECTION

The following case, in which a paravertebral injection was given for a proved unilateral calculus of the ureter, is presented as evidence of the location, intensity and direction of pain produced by irritation of the twelfth dorsal and the first and second lumbar nerves during the course

¹⁷ Pottenger, F. M. Symptoms of Visceral Disease, St. Louis: C. V. Mosby Company, 1930.

of the injection and the subsequent disappearance of previously mapped out areas of hyperalgesia on injection of procaine hydrochloride into the nerve roots. The injection is simultaneously a nerve-stimulating and a nerve-blocking process. The result is in agreement with the five postulates of Steindler¹⁸ for the establishment of a causal relation between local pain and radiation.

J. O., a man aged 36, was admitted to the Israel-Zion Hospital on Sept 16, 1937 with a history of three previous renal attacks. The first occurred in November 1936. The present attack began three days prior to admission, with sudden pains in the right renal region radiating to the pubis, the base of the penis, the testicle and the inner side of the thigh. The pain was intermittent and was accompanied by the usual symptoms of involvement of the urinary tract, including hematuria. The patient also complained of slight pain in the right hip, knee and ankle, and to a less extent of pain in the left knee and ankle and in the chest, particularly on the right side, on breathing. Urinalysis showed a 1 plus reaction for albumin, many red blood cells and occasional white blood cells. On cystoscopic examination an impassable obstruction was observed 5 cm from the right ureteral orifice, and roentgen examination revealed an irregular calcific shadow. Ureterotomy was performed on October 20, with removal of a calcium calculus 4 mm in diameter. On Jan 3, 1938 a nephrectomy was performed for chronic pyelonephritis with superimposed acute cortical abscesses and a urinary fistula.

On Sept 20, 1937, at 11 45 a m, Dr E. Salwen made a paravertebral injection of 2 cc of 0.5 per cent procaine hydrochloride into the roots of the twelfth dorsal and the first and second lumbar nerves on the right side. Owing to irritation of the nerve roots by the needles, the patient noted a "belt" of severe pain beginning at the site of injection and shooting downward, above the inguinal ligament, into the pubis, the head of the penis and testicle, along the inner aspect of the lower extremity, through the hip, knee and ankle joints and the popliteal region to the anterior and posterior parts of the great toe. It was accompanied by less clearly defined pain in the abdomen, extending anteriorly to about the ninth dorsal segment. In an area about the size of a silver dollar, corresponding to the region of maximum tenderness, mesial to the anterior superior spine of the ilium, the pain was so intense that the patient, as he expressed it, felt "as if something burst."

Table 5 represents the various hyperalgesic areas and points on the right and left sides (bilateral reflex) before and after blocking of the twelfth dorsal and the first and second lumbar nerve roots, on the right with procaine hydrochloride. The paravertebral injections were completed at 11 45 a m, and the following notes were made:

11 50 a m. There was no pain in the right lower quadrant. There was pain at the site of injection and in the penis.

12 00 noon. There was tenderness of the right rectus muscle. Tenderness was absent in the distribution of the ninth and tenth dorsal nerves and was plus-minus in that of the eleventh dorsal nerve. On the left side, tenderness was absent in the distribution of the ninth dorsal nerve, plus-minus in the area of the tenth and eleventh dorsal nerves and absent in that of the twelfth. There was no pain in the penis. There was slight burning on urination.

¹⁸ Steindler, A. Differential Diagnosis of Pain Low in the Back. All-
tion of the Source of Pain by the Procaine Hydrochloride Method. J. A. M. A.
110 106 (Jan 8) 1938.

12 10 p m There were no pains in the previously painful areas including the penis. The other intercostal nerves were considerably less tender.

12 20 p m There was no burning on urination. There was no pain or tenderness in the abdomen or the lower extremities. All the areas of the left intercostal nerves were normal except that of the seventh dorsal, in which there was a plus-minus response. The patient breathed more freely, with no pain in either side of the chest on deep inspiration. There was persistence of a point of mild maximum tenderness.

12 25 p m All the intercostal nerves were normal, including the left seventh dorsal nerve. There was no pain in either side of the chest, the abdomen or the lower extremities. All involved muscles were relaxed, including the posterior, lateral and anterior groups. The dorsal axial muscles were doughy to the touch,

TABLE 5—*Somatic Hyperalgesia Before and After Paravertebral Injections* in the Twelfth Dorsal and the First and the Second Lumbar Nerve on the Right*

	Right Side			Left Side		
	Before	After 30 Min	Following Day	Before	After 35 Min	Following Day
First lumbar nerve (near vertebra)	2--	—	1+	1--	—	±
Posterior to peak of crest of ilium	2--	—	±	±	—	—
Maximum point	3--	—	1--	1--	—	±
Inguinal belt	2--	—	—	±	—	±
Pubis	2--	—	—	—	—	—
Femoral triangle	1--	±	±	—	—	—
Popliteal space	1--	—	±	±	—	—
Medial malleolus	1--	—	±	±	—	—
Lateral malleolus	±	—	—	±	—	—
Rectus muscle—Medial edge	±	—	—	±	—	±
Body	2--	—	±	1--	—	±
Lateral edge	1--	—	±	—	—	±
External oblique muscle edge						
Upper part	1--	—	—	—	—	—
Lower part	2--	—	±	±	—	±

* Injection of 2 cc of 0.5 per cent procaine hydrochloride into the nerve roots

permitting distinct palpation of the surrounding bony landmarks. Prior to the injections all of these muscles had been spastic throughout.

At 9 00 a m on the following day, without any further medication or treatment the patient felt considerably improved. The tightness in his chest had disappeared entirely, and all pains were about 25 per cent less. Before the injections he had had shooting pains every ten to fifteen minutes, which were now gone. The abdominal pain and burning on urination had become only a smarting sensation. The pains in the chest, right hip, knee and foot had disappeared.

The irritation of the twelfth dorsal and the first and second lumbar nerve roots by the needles used in the injections reproduced the entire nerve reflex caused by a ureteral pathologic condition except the bilaterality. Subsequently, when the procaine hydrochloride injected

into these nerves produced the concomitant anesthesia of the zones previously found to be hyperalgesic a twofold purpose had been accomplished

The response of these structures to the injections requires further analysis. With reference to bilaterality, it may be said that although the injections were administered on the right side only, the reflex disappeared entirely on the left side also and remained considerably diminished on the day after the paravertebral injections. This evidence strongly suggests that the reflex on the side opposite the lesion may be due to spreading of the impulses from one side of the body to the other. The conclusion may be drawn, therefore, that a unilateral lesion may produce a contralateral reflex.

Three types of pain were felt: (1) muscular pain, which was dull and vague; (2) pain in an area the size of a silver dollar, corresponding to the point of maximum tenderness, and (3) radiating pain, which was sharp and well defined.

The following case is that of a patient presenting all of the ureteral hyperalgesic arcs who was given paravertebral injections by Dr. Sidney Immergut. Paravertebral injections were made separately into the left twelfth dorsal nerve on Aug. 12, 1934, into the left first lumbar nerve on August 14 and into the left second lumbar nerve on August 27. It was observed that after the injection into the first lumbar nerve root the hyperalgesia was considerably diminished, and the point of maximum tenderness dropped from 4 to 1 plus. After the injections into the twelfth dorsal and the second lumbar nerve roots, however, there was only a slight change.

The radiation of pain induced by faradic stimulation of the ureter by Ockerblad and Carlson¹⁹ corresponds in many respects to the irritation of the spinal nerve roots in the paravertebral injections.

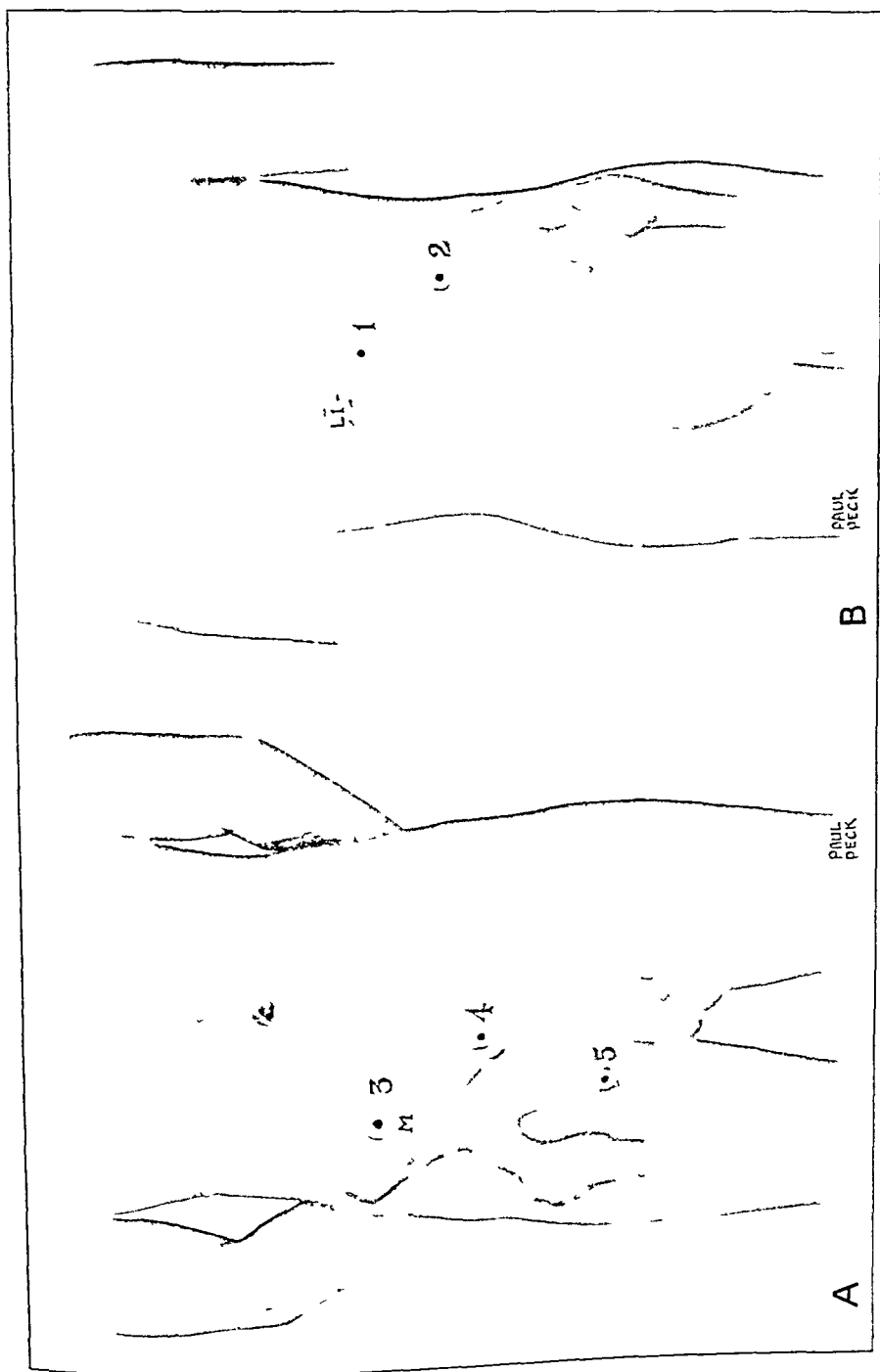
MECHANISM

The material presented in this report would be without point unless the mechanism of ureteral afferent nerve distribution were considered and hypotheses formulated concerning it. Such hypotheses can be based only on an analysis of the anatomicoclinical findings.

Cushing²⁰ after injecting cocaine into the ilioinguinal and iliohypogastric nerves noted that sensation disappeared in the oblique and transverse muscles. Lennander after division of the nerves in an incision through the sheath of the rectus muscle observed the mesial border of the incision to be without sensation. It is generally observed, further-

19 Ockerblad, N. F., and Carlson, N. E. Ureteral Pain as Determined by Faradic Stimulation in Man, *Proc. Soc. Exper. Biol. & Med.* **36**: 35 (Feb.) 1937.

20 Cushing, H. The Employment of Local Anesthesia in the Radical Cure of Certain Cases of Hernia, with a Note upon the Nervous Anatomy of the Inguinal Region, *Ann. Surg.* **31**: 1, 1900.



Tender points, (1, 2, 3, 4 and 5) in discoses of the renal pelvis and of the inter A, anterior view, B, posterior view
The point marked M indicates the point of maximum tenderness, that marked L₁, the first lumbar nerve

According to Libman - there are sensitive and hyposensitive persons, and the degree of sensitivity manifested is modified by whether the patients belong to one or the other category. Another variable factor is the severity of the morbid process. These two considerations must be recognized in an attempt to evaluate clinically the intensity and distribution of pain.

The following hypotheses may therefore be submitted:

1 The minimal and unilateral reflex is confined mainly to the twelfth dorsal and the first and the second lumbar spinal nerve. In the peripheral distribution, diffusion to outlying zones takes place by transmission of the impulses to adjoining nerves by way of nerve anastomoses and plexus formation.

2 In the minimal and bilateral reflex the invasion takes place additionally in the same spinal segment and on the contralateral side.

3 In the maximal reflex there is diffusion beyond its localized confines into the surrounding segments, that is, the chest, the upper part of the abdomen and the lower extremities, either unilaterally or bilaterally.

4 In cases in which bilaterality is present, the contralateral reflex is less intense than the reflex on the involved side. The greater the intensity of the stimulus on the affected side, the more frequently the bilateral reflex is present.

The extent of the entire reflex depends on the intensity of the impulse and the threshold of resistance.

The ureteral reflex has been observed in cases of gastric or duodenal ulcer, disease of the gallbladder and coronary attacks.

In conclusion, it may be stated that the initiation of the impulse is by way of the autonomic nervous system at the site of the stimulation, in the pelvis of the kidney or in the ureter, and that the impulse is transmitted afferently by peripheral distribution to the body wall by way of the twelfth dorsal and the first and the second lumbar spinal nerve. Diffusion may take place into higher and lower segments, either unilaterally or bilaterally by way of nerve anastomoses.

SUMMARY AND CONCLUSIONS

The relations of the iliohypogastric, ilioinguinal and genitofemoral nerves to the muscles of the trunk are reviewed and additional personal observations recorded. Plexus formation and anastomosis of the iliohypogastric nerve with adjoining spinal nerves and with the deep circumflex iliac artery were observed. A variation was noted in the point of emergence of the iliohypogastric nerve from the internal

oblique muscle. The aponeurotic intervals of the external and internal oblique and transverse abdominis muscles were found to vary in width.

Muscle spasm and tenderness were observed over the external oblique and the rectus abdominis muscle, and to a less extent over the intervening fascial space.

The upper limits of hyperalgesia were found to extend to the eighth or ninth dorsal spinal nerve or higher and the lower limits to the second lumbar nerve.

Five points of deep hyperalgesia were observed:

1. At the first lumbar nerve, near the spine of the vertebra.

2. In the posterior part of the iliac crest.

3. One inch (2.5 cm) mesial to and on a level with the anterior superior iliac spine (point of maximum tenderness). Normal anatomic variations were noted.

4. Above and lateral to the crest of the pubis.

5. Within the femoral triangle.

These tender points were frequently found on the side opposite the morbid process. In 14 of 17 cases, or 82.4 per cent, the lesions were localized by means of these points.

Joint pains which occurred during an attack of calculus of the ureter disappeared on alleviation of the attack.

"Tenderness along the course of the ureter" was found to correspond with tenderness along the lateral edge of the rectus abdominis muscle.

The contralateral reflex associated with a unilateral lesion was observed in 29.4 per cent of cases of calculus of the ureter. This is known as the "renorenal reflex."

A patient with calculus of the right ureter and bilateral physical findings received paravertebral injections of 2 per cent procaine hydrochloride into the twelfth dorsal and the first and the second lumbar spinal nerve root on the right side. A study was made of the tender points, areas and symptoms occurring bilaterally before and after the injections.

The mechanism of distribution of the afferent nerves particularly the peripheral, was studied from the anatomic and from the clinical point of view. The involvement of the twelfth dorsal and the first and the second lumbar nerve in diseases of the ureter was analyzed.

Hypotheses relative to the mechanism of the ureteral reflex are formulated. Consideration is given to (1) the minimal and unilateral ureteral reflex, (2) the minimal and bilateral ureteral reflex, (3) the maximal ureteral reflex and (4) the contralateral (bilateral) ureteral reflex.

MORBIDITY CAUSED BY OPERATIVE COMPLICATIONS

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In considering the value of any operative procedure, critical analysis of several factors is necessary. The mortality of the operation must be compared with the mortality of the disease for which it is performed, and the complications of the operation must be compared with the complications of the untreated disease. In a review of any series of operations it may be seen that both fatal and nonfatal complications arise, which are not inherent in the type of operation but may be sequelae of any surgical procedure. These include wound infections and pulmonary lesions. It is this group of postoperative complications that I wish to discuss in this paper. It has been said that all surgical procedures, no matter how simple, are attended by some risk of complications. As surgical science advances, the number of such complications will be reduced toward the minimum. During this evolutionary process, however, many prophylactic and therapeutic measures have been and will be suggested. These must be carefully weighed, the good ones being retained and the poor ones discarded.

Wound infections probably constitute one of the most common types of postoperative complication. In a recent survey of seventeen surgical teaching clinics,¹ I have found that there are almost as many methods in practice for the preparation of the operative field and the preservation of asepsis in the operating room. This might mean that all the methods are perfect, that none are perfect or that it is not known which is the best. The last is probably nearest the truth. The reason for this lack of knowledge is that studies of wound infection have been made, to a large extent, *in vitro* rather than *in vivo*. True statistical analyses have rarely if ever been made, but they are necessary to give proper weight to the many variables involved.

A similar problem confronted the obstetricians, who attempted to study the effects of their aseptic methods. For this purpose several of the local obstetric societies appointed commissions, who made a detailed

From the Department of Surgery, University of Illinois, the Department of Surgery, Cook County Hospital, service of Dr. J. Koucky, and the St. Joseph Hospital.

1 Beck, W. C. Preparation of the Operative Field. Report of a Survey of Seventeen Surgical Teaching Clinics, *Arch. Surg.* 33: 876 (Nov.) 1936.

study of the problem. They found that the first prerequisite was to define what constitutes morbidity in a given case and then to make this definition hard and inflexible for the purpose of comparative study. Not all of the various commissions active throughout the United States have adopted exactly the same definition, yet the material of each group is sufficiently large to make possible certain valuable generalizations.² Substandard methods of treatment have been recognized, and a definite reduction in maternal morbidity has been rendered possible. The problems of general surgery, because of their variety and complexity, are not so easily applicable to comparative study as are those of obstetrics. In the search for a method of study and statistical evaluation, however, the following analysis was carried out:

METHOD AND MATERIAL

In reviewing a rather large series of old charts, it was found that many of the complications which had evidently arisen were poorly recorded. This was true

TABLE 1—*Operative Complications*

Total number of cases with uncomplicated convalescence	332 (73.8%)
Total number of cases with complicated convalescence	118 (26.2%)
Total number without listed complications but with abnormal prolongation of fever	15 (3.3%)
Total number with complications but without abnormal prolongation of fever	6 (1.3%)

Report on 400 cases (thyroidectomy 70 cases, herniorrhaphy 145 cases, laparotomy 175 cases, miscellaneous [mastectomy, removal of tumors, sympathectomy, etc.] 60 cases.)

not only of the records in the private hospital but of those in the teaching clinics and charity hospitals. It was therefore necessary to work forward rather than backward in studying the cases. To do this adequately I enlisted the services of the senior surgical residents in the charity hospitals. They were given a 'complication sheet' to fill out for every case (table 1). This was done at the time of discharge of the patient from the institution. The records included a report of any preoperative complication, of the character and severity of the operation and of the postoperative complications. The type and rate of the pulse were recorded, and also the postoperative duration of tachycardia. The height of the postoperative temperature and the duration of any febrile reaction were recorded. In a small series of cases, total and differential counts of the leukocytes were carried out and correlated with the postoperative course. In another small series, determinations of the sedimentation rate were carried out during the postoperative period and correlated with the clinical course. Whenever there was doubt about the presence of complications, the interns' and nurses' notes were carefully reviewed for any possible clues. The latter proved illuminating in several cases in which it was recorded that the patient was coughing a great deal and expectorating large amounts of yellow mucus although there was no mention in the interns' progress notes of any pulmonary complication. In such cases either the record was discarded as incomplete or the attending surgeon was questioned.

² Cornell E., chairman of the Committee on Maternal Welfare Statistics, Chicago Gynecological Society. Personal communication to the author.

Whenever possible, some type of definition was coined for the different complications. Claude Beck's classification of wound infections was used so that an accurate analysis of the course of wound healing could be obtained. Only the obvious neurologic and psychiatric complications were listed unless consultation notes were available. The same held true for cardiac complications, so that possibly some of these were missed. Pulmonary complications were classed as bronchitis, bronchopneumonia, lobar pneumonia, massive collapse of the lung, atelectatic pneumonitis and embolic phenomena. Complications in the urinary tract were noted only when they were productive of fever, and caused obvious changes in the urine. For example, retention of urine demanding catheterization was not recorded. The recording of gastrointestinal complications was carried out only when such complications were of significant importance. Thus, postoperative "gas pains" do not appear in the records unless they were significant of inflammatory or obstructive ileus. Minor cutaneous manifestations, such as "sheet rash," were not recorded. Serious cutaneous conditions, e g, decubitus ulcers, were recorded.

For the purposes of this study, only operations performed in an uninfected field or those in which the danger of infection was presumably minimal were used. The inclusion of other operations would have complicated the problem too

TABLE 2—*Wound Complications*

Number of cases studied		450
Number of cases with wound complications		56 (12.4%)
Group I	1 case	(Secondary hemorrhage)
Group II	13 cases	(Sterile hematoma)
Group III	9 cases	(Infected hematoma)
Group IV	12 cases	(Mild infection)
Group V	17 cases	(Moderate infection)
Group VI	2 cases	(Serious infection)
Group VII	1 case	(Evisceration)
Group VIII	1 case	(Necrosis of edges)
Group IX	None	(Sinus or fistula)

much. For example, interval appendectomies and cholecystectomies for chronic cholecystitis were included, while similar operations for acute appendicitis and acute cholecystitis were not included. All of these should belong to group A according to Beck's classification (table 8).

The results of this investigation are not to be considered as evaluations of any standard or specific procedure. The operations were carried out in three different hospitals with the use of different technics and on patients of different classes. Two of the hospitals were charity institutions, and one was private. The operations were not all carried out by the same surgeons. The preparation of the operative field differed markedly in the three institutions and even in the same hospital with different operators. To obtain accurate, comparable statistics, certain definite rules must be observed, which will be formulated later in this article. It must be remembered that the statistics compiled here represent a composite picture.

In this series 450 cases were studied. As will be seen from table 1, the operations were divided into four groups: thyroidectomies, herniorrhaphies, laparotomies and miscellaneous procedures. The first two groups consisted of operations which were performed in tissue absolutely uninfected, while the latter two groups contained some in fields which might be considered as potentially infected for instance, appendectomies in the interval stage. No case of the invasion of a grossly contaminated field was included in the series.

The first object of the study was to find some criterion for the presence of a complication of the normal postoperative convalescence. For 15 patients, daily leukocyte counts were carried out during the first six postoperative days. One of the patients had severe bronchitis, and 2 had wound infections of moderate degree. The leukocyte counts of these 3 patients with complications were slightly higher than those of the normal patients. Eight of the patients, however, had elevated leukocyte counts for all of the period studied, and the difference in this respect between the complicated and the uncomplicated conditions was not found to be sufficient to warrant carrying out this procedure as a routine. In another series of 10 patients, the sedimentation rate was studied daily for a similar period. In this series there were 1 patient who had thrombophlebitis and 1 who had a moderate wound infection. All of these patients had accelerated sedimentation rates, but the rates for the patients with postoperative complications did not differ appreciably from those for patients with an uneventful convalescence.

It was noted that nearly all of the patients studied had a postoperative rise in temperature. The degree of the rise did not appear to be correlated with the severity of the operation or with the complication in the postoperative course. The status of the patient at the time of the operation did not appear to have any bearing on the height of the febrile reaction. The fever usually subsided by the third or fourth postoperative day. However it was noted that when a complication occurred the temperature almost invariably remained above 99.6 F after the fourth postoperative day or rose above this level during the postoperative course. Taking special note of this fact, I reviewed the histories of the patients who had been discharged as without complications and who had had a temperature above 99.6 F after the fourth day, and in most instances found an explanation. One patient was discharged from the hospital, after a supposedly normal convalescence, with a temperature of 100 F. He returned to the hospital eight days after discharge with a deep subfascial collection of pus which required evacuation. A second patient was returned to the referring physician, who reported evacuating several cubic centimeters of serum from the wound two weeks after discharge. When the case history was reviewed it was found that the patient had had a persistent febrile reaction during the postoperative course. As will be seen from table 1, in only 3.3 per cent of the cases in which there was a temperature of over 99.6 F after the fourth day could no cause be found. Some of these cases were in the earlier group, studied before we became aware of this phenomenon. In only 1.6 per cent of the cases was there a complication unattended by this rise in temperature. In none of the latter cases were severe complications present. In 1 of them there was a massive collapse of the lung which was immediately reduced.

The pulse rate did not appear to be significant. Many patients had elevations of pulse rate without any complication while others with severe complications had little or no elevation in the rate.

PREOPERATIVE COMPLICATIONS OR ASSOCIATED PATHOLOGIC LESIONS

It will be noted from tables 3 to 6 that the percentage of preoperative complications is very high. There are several reasons for this. Certain lesions were termed complications although they were a part of the disease for which the operation was performed. For example thyrotoxic heart disease was listed as a complication of hyperthyroidism. Similarly hypertension was listed as a complication in 2 cases in which splenectomy was performed for its relief. It is undoubtedly true

TABLE 3—*Complications Following Thyroidectomy (70 Cases)*

	Number	Percentage
Preoperative associated pathologic lesions	40	57
Thyrototoxic heart disease	36	51.4
Hypertension	2	2.8
Renal damage	2	2
Mild psychosis (coexistent with thyrototoxic heart)	1	1.4
Postoperative complications	11	15.7
Wound infection (group II, 2 group III, 1, group V, 1)	4	5.9
Thyroid crisis (mild)	2	2.8
Pulmonary complications	4	5.9
Auricular fibrillation	1	1.4

TABLE 4—*Complications Following Herniorrhaphy (145 Cases)*

	Number	Percentage
Preoperative complications	4	2.6
Pulmonary tuberculosis	2	1.3
Syphilis	2	1.3
Postoperative complications	22	15.2
Wound complications (group II, 3, group III, 2 group IV, 1 group V, 9)	15	10.3
Pulmonary complications	4	2.6
Urinary complications	2	1.3
Abscess on arm	1	0.7

TABLE 5—*Complications in Laparotomies (175 Cases)*

	Number	Percentage of Incidence	Percentage of Complications
Preoperative complications	26	14.8	46.9
Debility and cachexia	12	6.8	19.3
Severe secondary anemia	5	2.7	19.3
Dehydration	5	2.7	9
Cardiac lesions	2	1.1	4.5
Psychosis	1	0.5	4.5
Previous nephrectomy for tuberculosis	1	0.5	
Postoperative complications	67	38.2	
Wound infection (group I, 1 group II, 4 group III, 4, group IV, 9 group V, 7 group VI, 1 group VII, 1)	27	15.4	40.3
Pulmonary complications	15	8.5	22.4
Urinary complications	10	5.6	15
Inflammatory ileus	5	2.8	7.5
Cardiac complications	3	1.7	4.5
Thrombophlebitis	2	0.9	2.8
Furuncles and carbuncles	2	0.9	2.8
Decubitus ulcers	2	0.9	2.8
Subphrenic abscess	1	0.45	1.4

TABLE 6—*Complications in Cases of Miscellaneous Operations (60 Cases)*
(Mastectomy, Removal of Tumors, Sympathectomy, Etc.)

	Number	Percentage of Incidence	Percentage of Complication
Preoperative complications	8	13.3	27.5
Hypertension	3	5	57.5
Anemia	3	5	12.5
Cachexia	1	1.7	12.5
Diabetes	1	1.7	19.5
Pulmonary tuberculosis	1	1.7	
Postoperative complications	18	20	
Wound infections (group II, 4 group III, 2 group IV, 2 group VI, 1 group VIII, 1)	10	16.6	33.3
Pulmonary complications	5	8.3	
Cystitis	1	1.6	
Gastroenteritis	1	1.6	
Paronychia	1	1.6	

that only too often certain associated lesions remain unnoticed before the operation and are brought to light during the convalescence. This may be because of incomplete examination of the patient. On the other hand, certain of these complications are recognized and are not especially considered until they are aggravated or altered by the operative procedure. Thus, in 1 of the cases in which laparotomy (cholecystectomy) was done, a notation appeared in the report of the physical examination that the heart was enlarged and that there was a loud, blowing systolic murmur. On the third postoperative day the patient had an irregular pulse and an auricular fibrillation. No medical consultation had been held in this case, and it is possible, as the operation was not urgent, that medical care might have prevented this. Routine examination of the urine of surgical patients not infrequently brings to light diabetes. The case is then almost invariably considered in a special light, and surgical intervention is delayed for the proper care of the complication. Other preoperative complications should have the benefit of similar consideration.

TABLE 7—*Postoperative Days in Hospital*

Uncomplicated thyroidectomies	3.92 days*
Complicated thyroidectomies	6.84 days
Uncomplicated hemorrhaphies	10.2 days
Complicated hemorrhaphies	15.8 days

* Patients remaining in the hospital for social service disposal have been excluded.

Of the 450 cases studied, some preoperative complication was present in 78, or 15.3 per cent. As may be observed from table 2, 57 per cent of the patients on whom thyroidectomy was performed had preoperative complications. There were postoperative complications in 11 cases, in 8 of which there had been preoperative complications. This is as would be expected, i. e., a patient in whose case there are preoperative complications will have a more complicated postoperative course. Nevertheless, one should glean from such figures that, as precautions are taken in the treatment of preoperative complication, the frequency of postoperative complications will be reduced.

POSTOPERATIVE COMPLICATIONS

From table 1 it will be observed that of the 450 patients 332, or 73.8 per cent, had an uneventful convalescence, whereas 118, or 26.2 per cent, had some complication during the postoperative course. It is interesting that in no case was more than one complication noted. This may be due to lack of observation on the part of the person filling out the report but is more probably due to the fact that the presenting complication overshadowed the secondary one. There were 5 deaths in this series,

1 from a virulent infection, 2 from pulmonary embolism, 1 following an exploratory laparotomy for an inoperable carcinoma and 1 following an evisceration. This rather low mortality rate is probably due to the type of operations which were selected for this study ("clean" operations) and to the small number in the series.

It will be observed that two important complications have not been noted, surgical shock and "gas pains." The former probably did not occur, since the operation in the groups studied is rarely known to produce shock, although several gastric resections were included. Gas pains could not be included, as they are entirely subjective. Inflammatory ileus was observed in 5 patients. These had distention, silent abdomens and temperatures above 99.6 F. after the fourth day.

The largest group of postoperative complications is composed of complications related to the wound. In the series of 450 operations

TABLE 8—*Classification of Wound Healing (Claude Beck*)*

A	Clean surgical wounds
B	Potentially infected surgical wounds
C	Wounds in a grossly contaminated field
Subclassification	
0	Healing by primary intention
I	Secondary hemorrhage
II	Sterile hematoma
III	Infected hematoma
IV	Mild wound infections such as stitch abscesses, "seromas," erythematous wound edges
V	Moderate infections
VI	Serious spreading infections
VII	Eviscerations
VIII	Necrosis of the edges as in plastic operation
IX	subcutaneous dissections etc
	Persistent sinus or fistula

* Beck, C. Personal communication to the author.

there were 56 wound complications (table 8), i. e., after 12.4 per cent of the wounds showed abnormal healing (not all these wounds were infected). This is a very high figure, comparing unfavorably with the published statistics (with the exception of those published by Meleney in 1934). We believe that there are several reasons for this. The most important, in our opinion, is that the diagnosis of a complication referable to the wound was made after careful study of the wound rather than by study of the chart after the patient had left the hospital. All of the complications which occurred in the wounds were included, not only those which caused frank suppuration. Most of the patients were operated on in amphitheaters in the presence of students and visitors. Many of the visitors in the amphitheaters did not wear caps or masks.

3 Meleney, F. L. Infection in Clean Operative Wounds. *A New York Study, Surg., Gynec. & Obst.* 60:264, 1935.

but a glass shield⁴ in one of the hospitals separated them from the operation. In the other hospital there is no special shield for the prevention of droplet infection. The preparation of the operative field in the three institutions differed. In the first, the skin was prepared with a 6 per cent tincture of iodine or with the compound tincture, the excess being removed with alcohol. In the second, the skin was washed for ten minutes with sterile soft soap U S P (green soap) and sterile water, this was followed by application of the compound solution of mercuric chloride described by Vaichulis and Arnold⁵. In the third institution, the skin was washed with soap and water for five minutes, and mecresin⁶ was then applied. A comparative study will be presented in a subsequent report, for reasons outlined under statistical comparisons.

In this series the wound infections were incompletely studied from the bacteriologic standpoint. In the 2 cases of serious and spreading infection a hemolytic streptococcus was recovered. Cultures were obtained in only 2 of the cases of infected hematoma, in 1 of these *Staphylococcus albus* was recovered, while in the other a staphylococcus of the hemolytic type was found on culture.

It will be noted from table 7 that the largest group of wound complications resulted from hematomas in the wound. I have noted that when the edges of the wound are slightly raised and slightly reddened a hypodermic needle inserted into the wound will usually aspirate a small or moderate amount of old blood or of blood-stained purulent material. I therefore came to the belief that these were small hematomas rather than infections. The one evisceration occurred after an exploratory laparotomy in a debilitated and cachectic patient with an inoperable carcinoma of the stomach. There were no evidences of wound healing in this patient, and the wound was infected. The evisceration took place on the eighth postoperative day, and the patient died.

The next most common complication was pulmonary. As will be observed from table 9 most of the ailments in the group were classified as bronchitis. It was difficult to determine how many manifestations were necessary to justify a diagnosis of bronchitis but it was thought that a significant febrile reaction associated with cough and chest rales was sufficient. Whether or not this minor bronchitis represented small areas of atelectasis is not in the province of this discussion. There were 8

4 Some question as to the efficacy of the glass shield might be raised according to the researches of Wells F. Papers on Air Borne Infection Cambridge Mass. Harvard University Press, 1937.

5 Vaichulis I A, and Arnold L. A New Bactericide Surg, Gynec & Obst 61 333, 1935.

6 Mecresin (Upjohn) is composed of alcohol 50 per cent secondary amyl tricesols 01 per cent orthohydroxyphenyl mercuric chloride 01 per cent and acetone 10 per cent.

lesions definitely classified as atelectatic. Further study of this question is in order. Correlation with the modes of anesthesia was not carried out in this series.

In the entire series there were 13 patients, or 2.8 per cent, with complications referable to the urinary tract. There was usually mild cystitis, although there was 1 instance of violent cystopyelitis which resisted therapy. In reviewing the charts it was found that only 6 of the patients had had retention of urine requiring catheterization. The complication arose most frequently in young persons.

Thrombophlebitis of the femoral vein occurred in only 2 persons in the entire series. Both of these patients had varicose veins, and 1 of them had received several injection treatments of the veins before the operation. No definite predisposing factors other than this could be ascertained. In 1 of the patients the thrombophlebitis was mild and the patient's stay in the hospital was not greatly prolonged, while for the other patient hospitalization was prolonged to six weeks.

TABLE 9—*Pulmonary Complications*

Number of cases studied	400
Number of pulmonary complications	28 (6.2%)
Classed as bronchitis or tracheobronchitis	12
Classed as atelectasis or atelectatic pneumonitis	8
Classed as lobar pneumonia	1
Classed as bronchopneumonia	4
Pulmonary embolism	2
Pulmonary infarction	1

The other complications were so inconstant that discussion of them is scarcely indicated.

DURATION OF HOSPITALIZATION

The economic factor of operative complications is not inconsiderable. It is naturally important to determine how much longer the patients with complications remained in the hospital than those who had a normal convalescence. Today, when hospital insurance is becoming accepted, this factor will have to be taken into serious consideration. It also may be taken as an index of the severity of the complications. In this series only the thyroidectomies and herniorrhaphies are capable of comparison. As is seen in table 6, the average stay in the hospital for the patients in whose cases complications followed thyroidectomy was two and ninety-two hundredths days longer than for those with normal convalescence. For the herniorrhaphies the difference was five and five tenths days. This means that the patients on whom thyroidectomy was performed spent thirty-two and twelve-hundredths extra days in the hospital because of a complication, while those on whom herniorrhaphy was performed spent one hundred and twenty-three and two-tenths extra d

in the hospital. This figure would probably be much higher for a series of private patients, as such patients are often kept in the hospital until all evidence of the complication has disappeared. It is also worth noting that the complications following thyroidectomies and herniorrhaphies were mild and innocuous in comparison with those following laparotomies and miscellaneous operations.

COMMENT

It will be noted from the foregoing section that only the complications which follow surgical operations in general have been discussed. These are the ones which are often neglected and viewed with equanimity until some minor complication develops into a major one. When this occurs there is usually a general change in technic, followed by another period of quiescence until the next accident. I believe that surgeons should keep their technics in a constant flux, discarding the poorer methods for the better. This is possible only with comparable statistics. Many factors enter into the pathogenesis of the aforementioned complications. To evaluate any one of them all of the others must be kept at an absolute or relative value. For instance, in evaluating the comparative merits of silk and catgut for suturing infected wounds, the same type of patient must be used in all instances, the same surgeon must do the operating, preferably with the same team, the same operation must be done, the same preparation of the operative field must be carried out in the same operating room, the season of year should be the same, and the same draping and sterilization technic must be used. Above all, the series must be sufficiently large to obviate minor differences not noted. Therefore, this series is not a fit subject for comparison, as it is heterogeneous rather than homogeneous. It is reported, however, as possibly forming a base line from which further statistical study may proceed.

In reviewing the practical lessons learned from this study one finds that probably the most important is that an explanation can usually be found for a temperature which remains over 99.6 F. for more than four days. If one is alert for this sign one will be able to "pick up" far more of the complications which beset the surgical patient. If the complications are faithfully recorded a cause and a cure for some of them will undoubtedly be found.

It is also found that no single definition of a "wound complication" is possible. It is impossible to record that a wound heals by primary or secondary intention or to classify wounds by any such simple method. Rather, it is necessary to complicate the classification and study the wound healing process by analysis as is indicated in table 9.

Further, this study shows that complications may be studied by a quantitative as well as qualitative method. This can be done by the

determination of a normal duration of stay in the hospital. Patients who remain beyond this time *because of a complication* can be classified according to the period of time that they are hospitalized. Patients remaining in the hospital for study or for social or economic reasons cannot be included.

These criteria are more or less arbitrary. It would probably be best if the surgeons would emulate the obstetricians and through some surgical organization devise definitions of the various types of complicated convalescence and complicated wound healing. This would certainly be attended by some error, but in general the error would disappear with a large series. In this way accurate evaluations of the technics now in use would be possible.

SUMMARY AND CONCLUSIONS

1 It is absolutely necessary to use an accurate statistical method in evaluating the procedures used for the prevention and treatment of surgical complications.

2 Such statistics can be arrived at by securing arbitrary criteria for the presence of complications. It has been observed that a temperature of 99.6 F. for four or more days accompanies all but a small percentage of complications. In analyzing the value of any method, all other factors which may influence the result must be kept constant.

3 A series of 450 major surgical procedures has been analyzed from the standpoint of complications. This review has been made to demonstrate the feasibility of such a study rather than to offer comparable statistics.

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SIXTY-NINTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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LOS ANGELES

CONGENITAL DEFORMITIES

Osteopsathyrosis—Lippert¹ reports 3 cases of osteogenesis imperfecta. His patients were related, and in the same family there were 9 members with fragile bones. There was no biochemical evidence to show that the disease was related to pathologic absorption or retention of calcium or phosphorus. The treatment of the fracture was the same as that for normal persons. Rapid healing with callus formation was the rule. Administration of various drugs, vitamins and extracts did not affect the disease.

Humeral Varus—Burman² reports in detail a case of this rare condition. He states that only 8 cases have been recorded in the literature. The roentgen picture in his case was typical. The head of the humerus was in a varus position, so that the angle of inclination which is normally 130 to 158 degrees was reduced to less than 50 degrees. The tuberosities were elevated, the greater tuberosity was placed at a higher level than the head of the humerus, whereas normally it is about 6 mm lower. The epiphysal line was vertically rather

This report is based on a review of 147 papers selected from 224 titles relating to orthopedic surgery and appearing in the medical literature approximately between Nov. 1, 1938 and March 1, 1939.

1 Lippert, K. M. *Surgery* 4:762, 1938.

2 Burman, S. M. *Am. J. Roentgenol.* 40:682, 1938.

than horizontally placed. In such a case fusion may be premature, but is uncertain whether the rate of growth is greater in the upper or lower parts of the epiphysial line. This condition is due to an epiphysial injury sustained at birth or early in life. The patient in the case reported by Buiman was born by breech delivery with a known injury to the arm on the affected side. The uncommonness of the disease is explained by the following facts. First, it must be produced at birth by injury through breech delivery, second, it must injure the medial part of the epiphysial line so that its rate of growth is best at the outer part, and third, it must have a long enough period for its development. Treatment should consist of osteotomy "to correct the humerus varus of the head." In addition, fusion of the superior part of the epiphysial line may be considered in each particular case.

DEVELOPMENTAL DISEASE

Treatment of Essential Coxa Vara of Adolescents—Van Ness³ discusses under this heading the treatment of epiphysiolysis of the upper femoral epiphysis in 17 patients ranging in age from 11 to 17 years. There were 12 boys and 5 girls. Closed reduction was found to be unsatisfactory, the reposition being more apparent than real. Redressement alone was carried out for 8 patients. There was only 1 good result. In 2 patients ankylosis developed. In the remaining 5 there was limitation of motion. One patient, with early involvement, was treated only by abolition of weight bearing and the use of crutches, with a good result. One patient was treated with a traction caliper. This patient showed moderate limitation of flexion and rotation. Four patients were treated by osteosynthesis of the upper femoral epiphysis with a Smith-Petersen nail. The results were excellent in 3 cases and good in 1. The author advises this method in all cases in which there is not much displacement of the upper femoral epiphysis. When there is much upward displacement of the greater trochanter a trans-trochanteric osteotomy to produce relative coxa valga is recommended. This method has been used for 3 patients with excellent results and is preferred to an intra-articular operation.

Epiphysiolysis in Adolescence—Pomeranz⁴'s study is based on knowledge gained from a review of approximately 200 cases of slipped femoral epiphysis. He states the belief that no "preslipping stage" of the disease exists because when suggestive clinical symptoms are present there are always distinct roentgen features which indicate that slipping is taking place. In the early stages there are absence of the projecting

³ Van Ness, C. P. Bull. Soc. belge d'orthop. **11** 6, 1939.

⁴ Pomeranz, M. M. Am. J. Roentgenol. **40** 580, 1938.

"hump" of the capital epiphysis, increased width of the epiphysial line and subchondral resorption of the femoral neck. In the moderately advanced stages there is downward, inward and backward rotation of the femoral epiphysis with the femoral neck anteverted. In some of the treated and all of the untreated patients, union of the head and neck in the slipped position led to prominent changes which could be recognized later in life. Osteoarthritis is severe in cases of advanced involvement and may lead to permanent ankylosis of the hip. By experiments utilizing the hip of the monkey it was found that the increase in width of the epiphysial line is in reality produced by progressive anterior rotation of the femoral neck. The concentric defects seen in the roentgenograms represent the concurrent margins of the femoral neck and the epiphysis.

OSTEOMYELITIS

Acute Hematogenous Osteomyelitis—Key⁵ divides patients with acute hematogenous osteomyelitis into four groups. 1 Patients with mild infections who are not acutely ill. Early but not emergency drainage is advocated. 2 Severely ill patients with spreading infection but in good general condition. Immediate operation is advised unless the patient is under 3 years of age. 3 Severely ill patients in generally poor condition. Delay is advised until the general condition and the resistance can be improved. The interval, however, is a matter of hours rather than of days. 4 Patients in whom the infection has broken through the bone and whose acute illness is subsiding. Operation should be performed soon on persons in this group, but the condition does not constitute an emergency.

The reasons for these conclusions are clearly given and are based partly on the following findings: (a) under 2 years of age the organisms may be streptococci instead of staphylococci, (b) septicemia, if present, is due to infection in the osseous focus and not vice versa, and (c) mechanical localization of infection in the bone tissue is different. The conclusions are: 1 Early diagnosis is important, and each case should be considered individually on the principle that a deep abscess should be drained as early as possible. 2 Not every patient requires immediate operation but every patient presents an acute surgical emergency. 3 Early and adequate drainage in cases of acute osteomyelitis is the most effective means of preventing chronic osteomyelitis.

Osteomyelitis During the Period of Growth—Osteomyelitis in children is divided by Feure⁶ into three phases: the entry of the organism

⁵ Key, I. A. Rational Treatment of Acute Hematogenous Osteomyelitis. I. A. M. A. **111** 2163 (Dec 10) 1938.

⁶ Feure, M. Arch. de med. d. enf. **41** 695 1938.

the transportation of the organism and the development of a focus of infection in the bone. The author distinguishes five types of osteomyelitis: 1 Primary septicemic osteomyelitis. The initial blood culture yields bacteria, and there occurs a secondary infectious focus in bone. 2 Secondary septicemic osteomyelitis, in which the osseous focus is the source of the organism in the blood stream. 3 Pyemic osteomyelitis, with the formation of secondary foci in bone or in the viscera. 4 Acute frank osteomyelitis, without evidence of septicemia. 5 Resolving osteomyelitis, healing spontaneously without formation of pus.

There are two theories of the mechanism of acute osteomyelitis. According to Lannelongue's theory the bacteria localize in the metaphysis, where the circulation of the bone is most active during growth. Here the process involves simultaneously the marrow and the bone tissue, with secondary necrosis and sequestrum formation. According to Wilensky's theory the osseous necrosis depends directly on a septic embolus which obliterates one of the nutrient arteries of the bone. Systematic abstention from operation is rarely sufficient. Simple incision of the subperiosteal abscess often suffices for infants and young children. Opening the bone by drilling or by removal of a window is indicated in many cases. Resection of the bone is dangerous because of the possibility of failure of regeneration. Postoperative care should consist of good immobilization, often by plaster, with infrequent dressings.

Acute Osteomyelitis in Adults—The records of 9 cases of acute osteomyelitis in adults are reviewed by Zadek.⁷ Trauma and previous infection were noted in 3 cases. In adults the disease is slow and insidious but of gradually increasing intensity. The destruction is principally central and periosteal and is more likely to start in the shaft than in the metaphysis, since the blood supply of the bone is more evenly distributed in adults. The route of spread is chiefly through the central canal, and the development of a subperiosteal abscess is unlikely, owing to the firm adherence of periosteum to bone in adults. The shaft of the femur is most often involved. There may result a local area of periosteal bone production with pus formation and thickening of the shaft, but sequestrum formation is rarer. Culture showed *Staphylococcus aureus* in 7 cases and *Streptococcus haemolyticus* in 1. Pain is often not severe, the temperature is moderate or low, and the lesion may become chronic before the diagnosis is made. The lesion is not visible roentgenographically until it has been present for several weeks. Treatment should consist of removal of a window in the cortex followed by the Orr treatment. Case reports are presented.

⁷ Zadek, I. Acute Osteomyelitis of the Long Bones of Adults, Arch Surg 37 531 (Oct) 1938.

Pyarthrosis Due to Bacillus Haemophilus Influenza and Corynebacterium Xerosis—Weaver and Sherwood⁸ report 2 cases of hematogenous pyarthrosis due to influenza caused by *B. haemophilus*. Bacteriologic studies showed the presence also of *C. xerosis* in 1 of their cases. From their experience and a review of the literature they conclude that the disease occurs usually in infants and only rarely in adults. If it is not associated with influenzal meningitis the prognosis as to life and function of the joint is excellent but if such an association is present death usually occurs.

CHRONIC ARTHRITIS

Menopausal Arthralgia—Hall⁹ reports a series of 71 cases, the patients being women with arthritic symptoms beginning at an artificial menopause following castration. The patients were given estrogenic material intramuscularly in the form of estradiol benzoate (progyron B), 10,000 to 50,000 international units. Of 40 adequately treated patients suffering from arthralgia rather than true arthritis, over 70 per cent obtained almost complete relief of symptoms. Nine of 18 patients with true arthritis (atrophic, hypertrophic or mixed) were relieved of their symptoms. Hall states the belief that the rationale of estrogenic therapy is not merely restoration of ovarian hormones but the introduction of a substance which inhibits overactivity of the pituitary gland.

BACK

Spondylolisthesis—Meverding¹⁰ reviews 583 cases of spondylolisthesis involving the lumbar portion of the spine. The principal complaint was backache. The average age was 40, and 70 per cent of the patients were males. The condition most frequently occurs in persons engaged in heavy labor. Its origin is traumatic or congenital. Ten per cent of the patients had no complaints referable to the back. Fusion of the involved area is recommended if conservative treatment fails.

Lumbosacral Anomalies and Pain Low in the Back—Clarkson and Barker¹¹ enumerate the various anomalies which may be detected by careful roentgen examination of the lumbosacral area. The presence of these anomalies may be held accountable for pain in the lower part of the back. The technic of Williams and Wigby is advised. This

8 Weaver, J. B. and Sherwood, I. *Surgery* **4**: 908, 1938.

9 Hall, F. C. *New England J. Med.* **219**: 1015, 1938.

10 Meverding, H. W. *Spondylolisthesis as Etiologic Factor in Backache*. *J. A. M. A.* **111**: 1971 (Nov. 26), 1938.

11 Clarkson, W. and Barker, A. *South. M. J.* **31**: 515, 1938.

technic consists of carefully placing the patient so that in both the lateral and the anteroposterior view the central ray will pass vertically between the fifth lumbar vertebra and the first sacral segment. A typical abdominal and pelvic pain may be caused by lower segments of the spine. The authors mention 2 cases in which there was pain in the region of the gallbladder associated with anomalies at the lumbosacral region.

Surgical Treatment of Pain Low in the Back—Smith¹² states that it is the impression of the New York Orthopedic Group that the "pathology underlying painful backs lies far more frequently in the lumbosacral than in the sacroiliac joints. Assumption of the upright posture has placed undue strain on this area. Variations in the joints in this area, variations in the lumbosacral angle, posterior displacement of the fifth lumbar vertebra, laminal defects, spondylolisthesis, pseudosacralization and hemisacralization of the fifth lumbar vertebra and degeneration of an intervertebral disk are some of the causes of such pain. It is concluded that laminectomy and excision of the herniated disk is not always necessary, since elimination of motion in many cases is sufficient to relieve the irritation of the cauda equina. Ninety per cent of patients with pain in the lower part of the back are relieved by conservative measures. Operation is advised for 10 per cent. Five patients were operated on, the technic of Hibbs being used for spinal fusion. In the majority of cases the fifth lumbar vertebra alone was fused to the sacrum. Excellent or good results were obtained in 80 to 90 per cent. Analysis of unsatisfactory cases revealed either undetected arthritis or failure of fusion. Fasciotomy was used in 80 cases of sciatica. In many instances the pain was not relieved, but the procedure was of value in selected cases.

Compensation-Deviation Treatment of Scoliosis—Steindler¹³ states that when the compensation treatment for scoliosis was introduced twelve years ago the idea was to retrace nature's steps from the decompensated to the compensated stage on the supposition that if a natural arrest of scoliosis could occur in the state of compensation the same might be produced artificially by restoring this state. After twelve years of observation only 40 per cent of patients treated by compensation methods alone were able to maintain themselves in the compensated position without further progression of the deformity. Furthermore, it became evident that the success of fusion depends largely on the degree of spinal compensation obtained before fusion is carried out. When fusion was done before adequate compensation the position of fusion could not be maintained, but when fusion was carried out after

12 Smith, A. DeF. *Surgery* 4 13, 1938.

13 Steindler, A. *J. Bone & Joint Surg.* 21 51, 1939.

satisfactory compensation the state of compensation was maintained during the twelve years of observation. With the compensation treatment no absolute correction of any curve was accomplished. Since the spine is a column with three anteroposterior curves, lateral bending is impossible without rotation and rotation is impossible without lateral bending. Neither lateral pressure nor longitudinal traction, alone or combined, can produce correction, but derotation is an essential procedure, if not the most important prerequisite. The author states the belief that it is possible to straighten the lateral curve by derotation. This method of treatment consists of placing the patient in a Grieve chair while traction is applied or in a recumbent position on a derotating table. These pieces of apparatus were devised to enable one to mobilize the spinal column by rotation with the patient in both the sitting and the lying position. Between treatments the spine is prevented from collapsing by traction in recumbency or by a spinal brace with leg and head attachments. It would require a long time to determine the limitation of correction by derotation.

Kleinberg¹⁴ stresses early recognition of the deformity as the most important single factor in treating this condition. He states also that persistent and continuous treatment is necessary to attain a satisfactory result. He analyzes 221 private cases of structural scoliosis. After a consideration of the etiologic factors he discusses in detail the treatment of the condition. Each type of scoliosis is considered separately. Reduction of curvature of the spine may be obtained, the author states, either by a corrective plaster or Paris jacket or by application of traction on a convex frame. Illustrations of these methods are given in his paper. The former method permits the patient to be ambulatory, whereas the latter requires recumbency, but the former takes many months, the other only a few weeks. Traction on the convex frame is, in the author's experience, the simplest, quickest and most effective means of improving the scoliosis. The patient is placed in a convex frame, a Sayre halter is attached to the head of the bed and traction is applied. A pelvic girdle is put on, on each side of the girdle there is attached a band of webbing which extends to the foot of the bed. To each band a Buck's extension apparatus is attached for traction on the pelvis. With the patient recumbent, the muscles are relaxed and the deforming influence of the pull is eliminated by 5 pounds (2.3 Kg) of traction on the head and 5 pounds on each side of the pelvis. Each day 1 to 3 pounds (0.5 to 1.3 Kg) is added. Lateral traction may be added over the chest at the apex of the convexity. Within four to eight weeks the maximum improvement of the curvature is obtained. Additional expansion of the chest is brought about by using blow bot-

ties When maximal improvement is obtained, a corrective celluloid corset is applied and a long period of gymnastic exercises is recommended This part of the treatment lasts about two weeks The author feels that when carried out uninterruptedly it yields satisfactory results in about 80 per cent of cases Spinal fusion is advised for the remaining 20 per cent Also, he advises spinal fusion for paralytic scoliosis and for scoliosis causing persistent and disabling backache

NEOPLASMS

Primary Liposarcoma—Duffey and Stewart¹⁵ report a case of primary liposarcoma of bone arising in the femur of a 49 year old man The tumor was discovered after a second fracture, incurred while lying in bed Treatment consisted of high amputation, roentgen therapy and administration of Coley's toxins (erysipelas and erythrobacillus prodigiosus toxins) Later, owing to infection and recurrence of the tumor, disarticulation of the hip joint was performed Metastasis to the lungs was controlled by irradiation and administration of toxins A five-year follow-up showed the patient to be still well The tumor consisted mainly of spindle cells, with irregular groups of adult fat cells and small vacuolated fat cells The authors state the belief that the tumor was traceable to inflammatory changes in adult fat and therefore class it as a primary liposarcoma of bone

Primary Reticulum Cell Sarcoma of Bone—Seventeen cases of reticulum cell sarcoma of bone are reviewed by Parker and Jackson¹⁶ This type of growth constituted 77 per cent of primary bone tumors in patients under the age of 40 and in 35 per cent of primary bone tumors in patients under 20 It appeared most frequently in the long bones The clinical symptoms were the same as for the other types of primary bone tumor except that the patient's general health was better than would be expected with such a severe lesion In no other type of osseous neoplastic disease is such an extensive lesion so amenable to treatment In the cases reported the roentgen picture was not pathognomonic Histologically the tumor cells had round oval, indented or lobulated nuclei nearly the size of lymphocytic nuclei The chromatin was scattered and the amount of cytoplasm considerable Thirteen of the 17 patients were alive from one-half year to fourteen years after the onset of the disease, the other 2 died Three patients were treated by irradiation alone, 1 died, and the 2 others who had had neoplastic disease one to three years, were alive Of the 9 patients treated by amputation and irradiation 8 were alive from one-half year to fourteen years from the onset of the disease

15 Duffey, J. and Stewart, F. W. *Am J Path* 67:467, 1932

16 Parker, F., and Jackson, H. Jr. *Surg., Gynec & Obs.* 68:431, 1939

Ewing's Sarcoma—Geschickter and Maseritz¹⁷ studied 135 cases of Ewing's sarcoma. According to them, age, sex, duration of symptoms and systematic manifestations of the disease, while valuable adjuncts in diagnosis, are not conclusive findings. The tendency of Ewing's sarcoma to diminish rapidly under irradiation provides an important diagnostic feature, but this reaction is by no means specific, metastatic lesions and osteolytic sarcoma also respond to high voltage roentgen therapy, although not so rapidly. Roentgen diagnosis was possible in more than 70 per cent of the authors' cases, but the element of error could not be entirely eliminated, and the diagnosis necessarily rested in the last analysis on the microscopic findings. The points in differentiation between Ewing's sarcoma and similar lesions are discussed in detail and illustrated by roentgenograms. The resemblance between Ewing's sarcoma and subacute and chronic osteomyelitis still offers a serious problem. The similarity may be marked and may extend to the clinical factors of age, sex, rate, mode of rest, duration of symptoms and roentgen and physical findings. In 50 per cent of cases of Ewing's sarcoma as compared with 46 per cent of cases of osteomyelitis, the condition was found to occur in persons between 10 and 20 years of age, and in both conditions males were affected twice as often as females. Trauma played an equal role. The prognosis is grave, death occurred in 94 per cent of the cases in this series. The greatest problem is early and accurate diagnosis for which biopsy is necessary, irradiation as a therapeutic test, however, should precede biopsy. In proved cases resection of the entire shaft, when possible, is the operation of choice except for the weight-bearing bones of the lower extremity, for which amputation is advised.

Bone Sarcoma—Forty-seven patients with primary malignant tumors of the long bones (excluding plasma cell myeloma) were studied.¹⁸ These included 33 with osteogenic sarcoma, 8 with Ewing's sarcoma and 2 with reticulum cell sarcoma (4 patients refused treatment and were excluded from the series). The prognosis, judging by this series of conservatively treated patients with osteogenic sarcoma, is not as bad as is generally believed. In 28 cases in which amputation was performed, 11 patients or 39 per cent, were living without disease five years after the operation. The prognosis depends more on the amount of differentiation of the cells comprising the major portion of the tumor than on anything else. In 5 cases in which fibrous tissue predominated, amputations were performed and all the patients were well after five years. In 16 cases of the anaplastic type amputation

17 Geschickter C F, and Maseritz I H. *J Bone & Joint Surg* 21 26 1939

18 Simmonds C C. *Surg Gynec & Obst* 68 67 1939

was performed and only 1 patient was well after five years. Of the patients with Ewing's sarcoma, 4 were treated by irradiation and 4 by operation. All died.

NEUROLOGIC LESIONS

Pressure on the Brachial Plexus—Naffziger and Grant¹⁹ discuss 18 cases of the so-called scalenus syndrome, i. e., the signs and symptoms of cervical rib pressure on the brachial plexus without the presence of cervical ribs. Pain was the most common symptom, radiating into the hand in cases of severe involvement. Weakness was found only in cases of long-standing involvement. Symptoms could be brought on or increased in all cases by tensing the anterior scalenus muscle on the affected side. There was consistent tenderness over the insertion of the scalenus muscle on the first rib. One-half the patients showed evidence of disturbance of the sympathetic nervous system. The condition is believed to be due to anatomic and developmental factors that produced an abnormal position of the shoulder girdle in relation to the thoracic cage, among these are an embryologically "post-fixed" brachial plexus, injury, occupational strain and poor posture. Myotomy of the scalenus anticus muscle is required when postural treatment fails to relieve symptoms. In the authors' series the operative results were excellent, though recovery sometimes took several months.

FOOT

Bruce and Walmsley²⁰ state the opinion that the current clinical teaching on the arches of the foot is confusing and unsatisfactory. They have conducted a study of the architecture of the foot from the standpoint of development. Their observations satisfy them as to the presence of a longitudinal arch, but they can find no support for the theory of the presence of a transverse arch at the heads of the metatarsal bones. They state the opinion that pain in the metatarsal region is commonly due to splaying of the metatarsal heads with consequent strain on the transverse metatarsal ligaments. Such splaying may be due to decreased weight bearing on the head of the first metatarsal bone from congenital or other causes. The authors derive additional evidence for overstrain as a factor from the fact that dorsiflexion of the toes is often observed. Thus they conclude to be due to the unopposed contraction of the long and short flexor and extensor tendons in consequence of atrophy of the lumbricalis-interosseus system. For treatment they consider a metatarsal pad irrational. Relief depends on restoring the balance between the metatarsal bones and their load. The most important step is restoration of the functional activity to the lumbricalis-interosseus system,

19 Naffziger, H. C., and Grant, W. T. Surg, Gynec & Obst 67 722, 1933

20 Bruce, J., and Walmsley, R. Lancet 2 656, 1938

and preliminary correction of a dorsiflexion deformity of the toes is indicated. This is affected by tenotomy of the extensor tendons on the dorsum of the foot and of the contracted flexor tendons opposite the interphalangeal joints, followed by corrective fixation in plaster for several weeks.

[ED NOTE. This is an interesting and helpful study. Most orthopedic surgeons consider tenotomy of the extensor tendons of the toes a procedure likely to produce further deformity. Manipulation and exercises will usually overcome contracture.]

Osteochondritis of the Tarsal Navicular Bone—Brailsford²¹ distinguishes between osteochondritis in Kohler's disease, which occurs in the tarsal navicular bone in children between the ages of 2½ and 10 years, and osteochondritis of the tarsal navicular bone in adults. The characteristic lesion of the latter in the 9 cases reported occurred only in women. The process consists of an oblique splitting of the navicular bone and separation of the two fragments. The inner fragment gradually glides over the head of the astragalus to the medial side, and the outer fragment overrides the dorsal surface of the second and third cuneiform bones. In the later stages severe osteoarthritic changes develop in the normal midtarsal joint. These changes may be bilateral. In all 9 of Brailsford's cases there was bilateral involvement though the degree was not the same on both sides in every instance. The ages of the patients varied from 22 to 59. No conditions presenting similar roentgen appearances were observed by this author in men.

[ED NOTE.—Similar changes have been seen by several of the editors in roentgenograms of the feet in cases of osteoarthritis. Further study will determine whether this should be considered a separate entity or part of osteoarthritis.]

HAND

Purposeful Splinting of Injuries of the Hand—Koch and Mason²² emphasize the importance of rest in the treatment of injured tissues to secure muscular relaxation in cases of tendon injury and to bring constant tension on contractile scar tissue. They discuss application of splints for these purposes and illustrate the use of such splints by photographs and diagrams.

[ED NOTE. This is an excellent article describing many unique and useful appliances.]

Swollen Atrophic Hand—Oppenheimer²³ gives the clinical and roentgen findings in the cases of 14 patients in whom a peculiar swell-

21 Brailsford, I. M. *J. Bone & Joint Surg.* **21** 111, 1939.

22 Koch, S. L., and Mason, M. L. *Surg., Gynec. & Obst.* **68** 1, 1939.

23 Oppenheimer, A. *Surg., Gynec. & Obst.* **67** 446, 1939.

ing accompanied atrophy of the skin, the interosseus muscles and the bones of the hand. It was found to be correlated with unilateral bony constriction of the intervertebral foramina in the upper part of the cervical region of the spine on the side of the affected hand. The clinical syndrome was independent of the pathologic process which produced this constriction. In 6 of the 7 patients treated, cure was obtained by ultrashort wave therapy over the cervical portion of the spine. Atrophy of the bones was found to be correlated with atrophy of the skin but was independent of atrophy of the muscles. The author concludes that the development of well marked trophic lesions in an extremity affected for many years by rheumatic or arthritic pains seems to indicate that the pain may be due to radicular neuritis caused by chronic disease of the spinal column.

SHOULDER

Subacromial Bursitis—Rubert²⁴ describes a clinical, roentgen and statistical study of subacromial bursitis, with a review of 288 cases from the clinic of Arthur Steindler. This condition may be due to local trauma, direct or indirect, or to inflammation. In one group of cases it may be ascribed to general constitutional changes, such as arthritis, or to metabolic and nutritional changes. The pathologic process may be bursal and peribursal. The bursal changes consist of thickening of the walls, thickening of the synovial villi, exudation of fluid and adhesions. The peribursal changes are deposits of lime in the subjacent tendons due to injury or inflammation, with attempt at repair hindered by the poor blood supply of the region. Roentgenograms in several planes are important to rule out other possibilities, such as fracture and tumor, and to reveal the presence or absence of calcification. Codman's classification of subacromial bursitis is useful. 1 Acute spasmodic bursitis, with local evidence of inflammation, pain, tenderness and secondary muscle spasm. It may or may not show calcareous deposits. 2 Subacute adhesive bursitis, a result of progression of the acute spasmodic type. There is limitation of abduction and rotation but no severe pain. 3 Chronic nonadhesive bursitis, a further stage, with the adhesions gone but with residual roughening of the bursal walls. There is pain on motion in certain arcs as the roughened area passes beneath the acromion. 4 Bursitis due to complete tendon rupture.

Two hundred and eighty-eight cases are analyzed. The greatest age incidence was between 40 and 70. Five per cent of the patients showed local evidence of arthritis in the shoulder, differentiated from bursitis by the complete loss of motion and by the more obtuse angle between the scapula and the humeral shaft. The midpoint of arrest of

24 Rubert, S. R. Subacromial Bursitis. A Clinical, Roentgenographic and Statistical Study, Arch Surg 37 619 (Oct) 1938.

the shoulder due to arthritis is at 25 degrees of flexion and forward motion, so that when the arm is at the side the vertebral border of the scapula is no longer straight down but points medially in the midline. Injuries to the biceps tendon are differentiated by the limitation of forward and backward motion. In cases of acute involvement rest in abduction and external rotation, with use of heat and opiates, followed by mild passive motion as soon as possible, is indicated. Irrigation of the bursa with about 60 cc of procaine hydrochloride solution is a good form of therapy. Manipulation always gentle, is practiced to free adhesions if conservative treatment fails. Operative treatment for relief of tension and removal of calcifications and for tendon repair if the tendon is torn is confined to cases of acute involvement.

Periarticular Calcification of the Shoulder—Mallet-Guy and Frieh²⁵ review the subject of painful shoulders with calcification, restating Codman's observations and theories. The poor blood supply of the supraspinatus tendon plus the constant motion of the joint prevents proper scar formation and results in the deposit of calcium in the mass of necrotic fibers. Spontaneous perforation of the calcified deposit into the bursa is the rule, and this represents the process of the lesion. The particles are gradually absorbed by the fibrinous fluid secreted by the bursa and the bursa tends to return to normal save for adhesions and thickened villi. If perforation does not occur the reaction in the neighboring bursa may gradually subside, but there is danger of relapse and of chronic functional disability. The clinical features are variable. The roentgenogram may reveal calcification in both shoulders, one shoulder being symptomless. Treatment should be dominated by the idea that spontaneous healing is the rule. Immobilization in bed with the arm in abduction with periods of passive motion to prevent adhesions may be tried. Diathermy, infra-red rays and irradiation therapy may be used. Infiltrations of a local anesthetic combined with aspiration of the contents of the bursa is of proved value. Excision of the bursa should be a last resort.

MISCELLANEOUS

Plastic Surgery for Children—Straith and De Kleine²⁶ gave numerous examples of the psychologic effects of deformity in childhood, i. e., inferiority, shame, modifications of self expression and antisocial tendencies. The surgical care of such deformities is discussed but the main emphasis is placed on the medicopsychologic aspects. The conclusions are: 1. The importance of many deformities lies in the severe mental reactions and alterations of personality which result. 2. In the presence

25 Mallet-Guy, P. and Frieh, P. *Rev. d'orthop.* **26**: 20, 1939.

26 Straith, C. L. and De Kleine, E. H. *Plastic Surgery in Children*. Medical and Psychologic Aspects of Deformity. *I. A. M. A.* **111**: 2364 (Dec. 24) 1938.

of deformity the most important single factor is surgical restoration to normal at the earliest possible date 3 Whenever possible deformities in children should be corrected before school age

[ED NOTE—Most of the examples used in this article did not fall strictly under the head of orthopedic surgery, being cases of cleft palate, deformities of the nose and similar conditions, but the general conclusions concern the orthopedic as well as the plastic surgeon]

OPERATIONS ON BONES AND JOINTS

Surgical Repair of the Long Disabled Hand—Young²⁷ reviews known principles in the surgical repair of hands long disabled owing to infection or to trauma in skin, subcutaneous tissue, tendons, tendon sheaths or joints He stresses asepsis, adequate preoperative care of the skin, proper placing of cutaneous incisions and accurate hemostasis He states that he has never had a recurrence of a surgically treated Dupuytren contracture after complete removal of the fibrous aponeurosis, complete hemostasis, grafting of skin flaps and immobilization of the fingers in extension during healing

Chronic Synovitis Treated by Synovectomy—Inge²⁸ reviewed 86 cases of synovectomy of the knee joints followed from one-half to five and one-half years Synovectomy for specific lesions, such as tuberculosis, echinococcic disease, osteitis of the tibia and hemangioma, failed in all cases The conditions in the remaining 77 cases were divided into rheumatoid arthritis, osteoarthritis and chronic synovitis (the latter including 9 cases of trauma and 6 of osteochondromatosis) The conclusions drawn were 1 In properly selected cases of nonspecific proliferative synovitis, synovectomy offers a 95 per cent chance of improvement and a 60 per cent chance of restoration of a practically normal joint 2 Patients with osteoarthritis with secondary synovial hypertrophy have a 90 per cent chance for improvement 3 In this series, patients with rheumatoid arthritis were relieved in only 50 per cent of cases, and the knees of some were made worse 4 Failures were due to improper selection of cases The rules for the proper selection of cases suggested by Swett and Jones in 1923 are still valid

[ED NOTE Synovectomy carefully performed with attention to hemostasis and with early motion in the joint is a useful procedure for quiescent arthritis When the arthritis is active, support of the joint and roentgentherapy are far safer]

27 Young, F Surg, Gynec & Obst **67** 273, 1938

28 Inge, G A L Eighty-Six Cases of Chronic Synovitis of the Knee Joint Treated by Synovectomy, J A M A **111** 2451 (Dec 31) 1938

Hoke Operation for Flatfoot—L'Episcopo and Sabatelle²⁹ report on a series of 16 patients on whom operation for flatfoot was performed. The procedure was essentially that devised by Hoke in 1931 except that an attempt to fuse only the first cuneiform and navicular bones was made and that in some cases the heel cord was lengthened. The average age of the patients was 13 years, the youngest was 7 and the oldest 19. The operation was performed only on patients with flaccid flat feet associated with pain or fatigue or both and in whom the symptoms were static. No cases of arthritis were included. The follow-up period varied from eight months to three years. The results were good in 68.7 per cent and fair in 31.3 per cent of cases. The authors felt that the operation was definitely indicated in a well selected group of children with flaccid flat feet. It seems that bony union is not essential for good results. Some patients were definitely relieved in spite of fibrous union.

Restoration of Muscle Balance in the Treatment of Obstetric Paralysis—L'Episcopo³⁰ finds that the shoulder joint in obstetric paralysis of the upper part of the arm is not adducted, there are slight posterior dislocation of the head of the humerus and torsion of the upper part of the humerus. Because there is marked muscular imbalance with a tendency of the pectoralis major, teres major, subscapularis and latissimus dorsi muscles to shorten, he has devised a method of transplanting muscles to secure better muscular balance. Two incisions are made, along the anterior and along the posterior margin of the deltoid muscle. The teres major and the latissimus dorsi muscle are freed from the medial aspect of the humerus. The contracted anterior articular capsule is then cut to permit outward rotation of the humerus. The teres major and latissimus dorsi muscles are brought about the under side of the humerus and fixed to an osteoperiosteal flap on the lateral side of the humerus. The author has performed the operation on 15 patients with obstetric paralysis and on 1 patient with spastic paralysis. The 15 patients with obstetric paralysis all showed marked functional improvement.

FRACTURES AND DISLOCATIONS

Fracture-Dislocation of the Spine—Of 259 patients with injury to the spine admitted to the hospital over a five year period, 80 had symptoms referable to the spinal cord or to the nerve roots. The group with injuries to the cord were discussed by Coleman and Meredith,³¹

29 L'Episcopo, J. B., and Sabatelle, P. E. *J. Bone & Joint Surg.* **21**: 92, 1939.

30 L'Episcopo, J. B. *New York State J. Med.* **39**: 357, 1939.

31 Coleman, C. C., and Meredith, J. M. *Treatment of Fracture-Dislocation of the Spine Associated with Cord Injury*, *J. A. M. A.* **111**: 2168 (Dec. 10) 1938.

the following conclusions being reached 1 Laminectomy is indicated only in cases in which the cord is compressed but not destroyed 2 If lumbar puncture shows no block, operation is not indicated If block is present, operation is indicated only if it seems that the cord possessed some ability for repair 3 If lesions of the cord produce immediate complete interruption, operation is futile 4 Reduction of cervical dislocations does not improve the prognosis of injury of the cord but sometimes helps root symptoms 5 Severe but incomplete lesion of the cervical segment of the cord should be treated with traction for twenty-four hours, if no improvement occurs, laminectomy should be done 6 For severe incomplete dorsal lesions immediate laminectomy is advisable 7 Prompt laminectomy is indicated for complete lesions of the cauda equina

Recurrent Dislocation of the Shoulder—Twenty-five cases of recurrent dislocation of the shoulder in which operation was performed by a number of different surgeons according to the Nicola technic were collected by Horwitz and Davidson³² Twenty cases have been used as the basis of this study The postoperative period varied from six months to eight years at the time this study was made There were 17 successful results and 3 recurrences In 1 of the cases in which dislocation recurred there was a violent injury, and at operation a rupture was found of the spanning portion of the tendon in the joint In a second case of recurrence the shoulder felt stronger and the dislocations were less frequent after the operation In the third case of recurrence following the Nicola suspension there was a hiatus in the deltoid muscle due to stripping of the attachment of this muscle at the time of operation There was abnormal mobility of this muscle at the time of operation There was abnormal mobility of the humeral head indicating excess length of the tendon due either to stretching or to improper attachment of the tendon in the osseous tunnel Also, the disturbance in growth caused by drilling across the epiphysal plate in a child of 12 years may have disturbed the mechanics of the new intra-articular ligament

Transcondylar Fractures in Childhood—Dunlop³³ discusses the treatment of a type of fracture which involves the lower end of the humerus in young children It is most prevalent between the ages of 5 and 12 years The fracture passes across the broad distal end of the humerus and through the thick portion of the bone known as the olecranon and the coronoid fossa The distal fragment remains in one piece The lesion has been called by some authors an epiphysal separation However, there is no epiphysal line at this level of the bone

32 Horwitz, M. T., and Davidson, A. J. *Surgery* 4:74, 1938

33 Dunlop, J. J. *Bone & Joint Surg* 21:59, 1939

although there is one distal to the line of fracture. Traction by adhesive tape is applied to the arm up to the elbow joint, treatment is continued by gradual straightening of the arm and attachment of weight to the traction apparatus, which is similar to a Buck's extension applied to the side of the bed with a pulley. Elevation of the side of the bed toward the traction or the attachment of a sheet about the body of the patient may be necessary to prevent him from being pulled out of bed. One-half hour after the application of traction roentgenograms should be taken to determine the amount of weight required and the necessity for a counterweight with a sling over the upper part of the arm. An additional roentgenogram should be taken in three to four hours to determine whether there should be an increase in the amount of weight used or a change of the angle of pull. When the roentgenogram reveals sufficient callus, traction is removed and a posterior plaster is applied. A sling is given with the elbow flexed at right angles. The child is then allowed to go home with the arm in the sling. In three to four weeks the splint is removed. The arm is tied to the neck with a cravat sling, and motion is started. It is unwise to force straightening of the elbow. A normal elbow should result in three or four months.

Neurologic Lesions in Recent Fractures of the Lower End of the Humerus—Sorrel and Sorrel-Dejerine³⁴ review 252 cases of recent fracture of the lower end of the humerus, in 21 of which the condition was complicated by injury to one or more nerves. There were 207 supracondylar fractures, 23 fractures of the internal epicondyle and 22 fractures of the external condyle. Of the 207 supracondylar fractures, there were 23 of the internal epicondyle and 22 of the external condyle. Of the 207 supracondylar fractures, there were 23 of the flexion type of fracture, and in these 23 the ulnar nerve was involved 7 times, an incidence of 30 per cent. The mechanism of the neural injury is described as follows: the nerve, being flexed in the groove of the olecranon, is pulled forward with the distal fragment of the humerus. This produces angulation of the nerve on the proximal fragment, resulting in paralysis. In none of these 7 cases of ulnar paralysis was the nerve actually torn. In 4 cases the paralysis was noticed only after removal of the plaster, at operation the nerve was found to be pressed on by a spur from the proximal fragment and was not involved in callus. In 1 instance the nerve was crushed between the fragments. On the average, recovery of the nerve begins from eight days to three weeks after operation with complete recovery in six to eight months. It is safe to wait up to fifteen days for signs of recovery of the nerve before operation is undertaken. If the reduction is not satisfactory, however

34 Sorrel E. and Sorrel-Dejerine (Mme). *Rev. d'orthop.* 25: 609, 1938.

operation should be done early. Associated with the 184 supracondylar fractures of the extension type "there were 4 instances of radial paralysis (2.1 per cent), 4 of median paralysis (2.1 per cent) and 1 of combined median and ulnar paralysis." The mechanism was stretching of the median and radial nerves over the proximal fragment by the backward displacement of the distal fragment, but the nerves were protected in most instances by the cushion of the brachialis muscle so that they were infrequently injured. For paralysis of the radial nerve 3 operations were done. In 1 case the nerve was found severed, in the other 2 it was only pressed on and flattened. In the fourth case the paralysis disappeared soon after a good closed reduction. The authors advise operation at the end of fifteen days if there is no improvement. Paralysis of the median nerve was accompanied in each case by signs of vascular compression, with absence of the radial pulse signs of an impending ischemic contracture. In 3 of these cases immediate operation was done, which revealed marked compression of the vascular bundle and the median nerve, caused by protrusion of the proximal fragment through the torn brachialis muscle. In the fourth case a Kirschner wire was placed through the olecranon, producing an excellent reduction, and all symptoms rapidly disappeared. In the 1 case of paralysis of the median and the ulnar nerve together the weakness was noticed forty days after a good reduction by an open operation. The paralysis disappeared one month later. There were 25 fractures of the medial epicondyle with 4 lesions of the ulnar nerve, an incidence of 17.4 per cent. Three of the fractures were accompanied by dislocation of the elbow. In 2 of the dislocations the epicondyle and the nerve were caught in the joint after reduction of the dislocation. Operation should always be done in such circumstances. In 3 of the patients full return of function required six to seven months, 1 patient could not be followed. There were 22 cases of fracture of the external condyle with 1 instance of paralysis of the ulnar nerve. In this case a large fragment was torn off, accompanied by a complete lateral dislocation of the radius and ulnar nerve. Two and one-half months after the operation recovery was complete. In the remaining case the ulna was transfixed by a Kirschner wire. There were no immediate symptoms, and the paralysis was discovered only after removal of the plaster. Two months later operation was done and the nerve was freed from adhesions. Complete recovery required fourteen months.

Late Rupture of the Extensor Pollicis Longus Tendon After Colles' Fracture—Blount³⁵ reports 2 cases of rupture of the tendon of the extensor pollicis longus muscle after Colles' fracture. One patient was a 44 year old janitor in whom rupture of the tendon occurred two

35 Blount, W. P. Wisconsin M. J. 37:912, 1938

months after the fracture. The other patient was a seamstress 56 years old in whom rupture of the tendon occurred three weeks after injury. Rupture of the tendon occurs from injury to the mesotendon and interference with the blood supply as a result of the fracture. Pain is frequently absent, the patient becoming aware of the injury when there is inability to extend the distal phalanx of the thumb. Rupture of the tendon occurs several weeks to several months after the patient has returned to work. Tendon suture is easily performed if treatment is sought early. In cases of neglect a tendon graft may be required. This is a rare complication of Colles' fracture. A review of the literature is given.

Fractures of the Neck of the Femur—Putti³⁶ discusses in detail the types of fracture of the hip but limits his discussion of therapy to intracapsular lesions. He states the belief that a lag screw supplies a positive opposing factor in immobilizing these fractures, whereas a Smith-Petersen nail acts only as a passive internal splint. All the operative stages utilized in inserting the steel lag screw are well described and illustrated. A portable roentgen unit with two tubes on one stand is used so that anterior, posterior and lateral roentgenograms may be taken repeatedly as desired without shifting the tube or changing the position of the patient on the traction table. A 4-inch (10 cm) lateral incision is used. The following statistics are given. Cases of fractured hips treated in the Institute Rizzoli up to 1937 included 698 cases in which treatment by reduction and plaster was used. In 529, or 75.7 per cent, the fractures are reported as healed. Though the Smith-Petersen nail has been used, this series is not reported. Of 34 fractures for which the lag screw was used, 9 were subcapital fractures, 23 were transcervical fractures and 2 were fractures through the base of the neck. The screw was introduced in 31 cases between the fifth and the thirtieth day, in 1 case after five months and in 1 after seven months. The preliminary reduction was accomplished by cutaneous traction with the patient in bed, the extremity being abducted and internally rotated with slight flexion. The results are based on 32 cases, the patients in 2 being still under treatment. Four patients, or 12.1 per cent, died. Excluding the 4 who died and 3 who did not return, the results are classified as follows: in 17 cases, or 68 per cent, excellent (bony union), in 5 cases, or 20 per cent, good (stable joints), and in 3 cases, or 12 per cent, poor. Roentgenograms are shown in 19 cases, in 15 instances showing obvious osseous union and excellent anatomic position. Incidentally, after fixation with the lag screw a plaster spica was applied, this was "bivalved" after the first month to allow physical therapy and was removed after the second month. A brief report was also made of

21 cases of nonunion, the earliest two and one-half months and the latest twenty-one months after operation, treated by intertrochanteric osteotomy. One patient died, in the case of another abduction was inadequate. All of the remaining 19, however, had satisfactory results, 3 roentgenograms shown proving bony union. Satisfactory results were obtained in treatment of pseudarthrosis.

[ED. NOTE—The article is excellent, but it is not a convincing argument for the lag screw. In the first place, immobilization required accessory plaster spicas. In the second place, the incidence of union is not high as compared to recent results in America, where the Smith-Petersen nail has been used.]

Treatment of Fractures of the Ankle—In this paper Campbell³⁷ describes in detail the various types of fractures of the ankle. He divides them into two main classes, major fractures and minor fractures. In the author's opinion, treatment of the former by means of a skin-tight walking plaster cast can hardly be improved on. Minor fractures, he states, are often given treatment neither necessary nor advantageous. Minor fractures are those in which only one side of the joint is involved. Such fractures are considered invariably stable. Involvement of both sides does not necessitate a fracture through bone on each side, a tear of the lateral ligament combined with a fracture on the other side being sufficient to place the lesion in the group of major fractures. In the treatment of minor fractures the author has adopted Leriche's method of local anesthesia by infiltration with procaine hydrochloride. The pain is abolished, and the patient is allowed to walk home without support. He is seen the next day, as occasionally a second infiltration is required. He is encouraged to resume his normal activity. Roentgenograms are taken from time to time until bony union occurs. The author reports in detail a series of 18 cases in which treatment was conservative, in none of these has displacement or nonunion been found to result.

RESEARCH

On Fascia Grafts in Tendon Defects—This is a study³⁸ to determine whether dead fascia used to fill tendon defects will or will not act as a foreign body and whether or not absorption occurs. Previous studies by Nageotte and Sencert have shown that the dead cells of a graft are removed by wandering cells from the host, after which fibroblasts from the host grow into the preexisting connective tissue framework of the graft and repopulate it with living cells. In 25 dogs a

37 Campbell, W. G. *Lancet* 2: 872, 1938.

38 Weinberg, E. D. Dead (Ox) Fascia Grafts in Tendon Defects. An Experimental Study, *Arch. Surg.* 37: 570 (Oct.) 1938.

section of the tendon in the foreleg was removed and on tascia preserved in 70 per cent alcohol was sutured to the stump ends. The dogs were killed at intervals varying from eleven to two hundred and eighty-five days, and the tendons were studied. It was found that the ends of the graft became traved out and edematous and were invaded by an ingrowth of young fibroblasts. These fibroblasts later worked their way into the interior of the graft, so that after forty-two days little evidence of the dead graft as such remained. There was no foreign body giant cell reaction around the silk sutures. The preserved fascia was well tolerated and in time there was such a complete substitution that it was difficult to tell that the graft had ever been dead.

Use of Hydrochloric Acid in Delayed Calcification of Fractures—Cornell and his associates³⁹ report the clinical and roentgen observations in 5 cases of fractured bones in which excessive atrophy of bone and delayed calcifications were found about the site of fracture. Observations suggested that the osseous atrophy was the result of some metabolic or constitutional disturbance affecting the intestinal absorption and subsequent utilization of calcium salts and was thus responsible for the delayed calcification. The evidence indicated that the disturbance was due to decrease or absence of hydrochloric acid in the stomach. Calcium salts are soluble in acids and relatively insoluble in an alkaline medium. Intestinal acidity is due to hydrochloric acid in the stomach to the fatty acid formed during digestion and to lactic acid fermentation. Vitamin D also is associated with the production of intestinal acidity. Telfer's experiment led him to state that absorption of calcium is initially dependent on the free hydrochloric acid in the stomach. The use of hydrochloric acid without the proper calcium intake may be harmful since hydrochloric acid besides furthering the utilization of calcium, increases excretion of this substance. Analysis of the gastric contents was carried out in 20 cases of fractures and in 12 of these the findings were normal and normal healing occurred. In 8 cases gastric acidity was either absent or low and was associated with a diminished volume of gastric content. In these 8 cases healing did not occur with the usual method of treatment. The authors conclude that the addition of hydrochloric acid (4 to 8 cc. of a 10 per cent dilution three times a day) to a diet high in calcium and vitamins increases the absorption of calcium and furthers the calcification of bone.

Bone Regeneration—Levander⁴⁰ has endeavored to find a reason for the metaplastic theory of bone formation, i. e., the transformation of connective tissue into bone tissue. He has studied the mode of

39 Cornell L. W., Bernheim A. R. and Person E. C. J. Bone & Joint Surg. **21**: 40, 1939.

40 Levander H. Surg. Gynec. & Obst. **67**: 705, 1938.

origin of new bone after transplanting into soft parts hard bone tissue stripped of periosteum. This new bone seemed to be formed from mesenchymal tissue about the graft but not necessarily in contact with it. Alcoholic extracts of bone tissue were injected into soft structures, and in 22 per cent of instances cartilage or bone was formed. After control injections of alcohol alone no bone was formed. The author concludes that bone regeneration takes place as the result of some specific bone-forming substance activating the nonspecific mesenchymal tissue.

Calcification of Hyaline Cartilage—Falconer⁴¹ examined costal, tracheal and bronchial cartilage taken from old persons with reference to the occurrence of calcium. In only 41 of 200 cases was the cartilage macroscopically free from calcium, but in many of these cases microscopic calcium deposits were observed. There are three different ways in which calcium settles in the cartilage: (1) as a diffuse distribution of small kernels, (2) like a capsule around the dying cartilage, and (3) in the form of strands which traverse the interstices between the endoplasmic areas in the exoplasm.

Roentgen Appearance of the Ligaments of the Knee Joint—Lindblom⁴² has been able to demonstrate the ligaments of the knee joint by the injection of perabrodil (skioldan), a water-soluble radiopaque substance, into the knee joint. If there was effusion within the joint preliminary aspiration was done. About 15 cc. of 4 parts of perabrodil and 1 part of 0.5 per cent procaine hydrochloride was injected. Stereoscopic lateral roentgenograms were taken with the knee flexed 90 degrees, and anteroposterior roentgenograms, with the knee flexed 50 degrees. Lesions of the cruciate ligaments and of the tibial collateral ligament could be demonstrated.

Roentgen Diagnosis of Destructive Lesions of the Knee Joint—More than 190 defects of varying size and location were produced in the bones about the knee joint by Lachmann⁴³. These involved the cortex and the spongiosa separately and in combination. The results revealed that not all osseous defects are visible on the roentgenogram in either frontal or profile views unless they are of minimum size. The dimensions necessary for visibility vary with the location of the defect. Conoid excavations involving only the spongy structure require a diameter of from 0.5 to 1.7 cm. at their base and a depth of from 0.5 to 0.9 cm. Disklike cortical defects must have a diameter of from 0.5 to 2 cm. in order to be seen, the factors determining visibility of a defect

41 Falconer, B. *Calcification of the Hyaline Cartilage in Man*, Arch. Path. 26: 942 (Nov.) 1938.

42 Lindblom, K. *Acta radiol.* 19: 582, 1938.

43 Lachmann, E. *Radiology* 3: 521, 1938.

are (1) direction of its longest axis in relation to the central x-ray beam, (2) the diameter of the transradiate forms superimposed over the defect, (3) the relative amounts of cortical and spongy matter in the overlying bone, (4) the distance of the defect from the tube and the film, (5) the character of the border of the excavation, (6) the content of the defect, and (7) the state of calcification of the surrounding bone. In the light of these results the limitations of roentgen diagnosis in deep infections frequently involving the knee joint are pointed out. For example, special attention is called to the fact that a normal roentgenogram does not exclude the possibility of tuberculosis of the knee joint and that the roentgenogram gives a picture of the stage, prognosis and progress of the disease only with certain reservations, none of the classic roentgen signs of tuberculosis in itself being typical of this infection. In regard to osteogenic sarcoma, it is pointed out that this infection may be present with normal findings and that no roentgen sign of osteogenic sarcoma is absolutely characteristic. In regard to osteochondritis dissecans, it is pointed out that the first stage of this condition escapes roentgen diagnosis. Later phases of the disease may be visible, but this depends on the width and position of the radiolucent ring around the necrotic bone fragment. In this study, for example, when the line of demarcation did not exceed 1 mm the front view was normal and the side view showed only a faint interrupted outline of parts of the fissure surrounding the fragment.

News and Comment

International Congress of European Society of Structive Surgery—

The fourth international congress under the auspices of the European Society of Structive Surgery will be held in Paris, October 5 to 7. The honorary president of the congress is Prof P. Sebileau, member of the Academy of Medicine of Paris, and the president is Dr L. Dufourmental. The following two subjects will be discussed: (1) treatment of destructions and deformities resulting from scar retraction of the eyelid, (2) treatment of deformities of the jaw. There will also be presentation of other communications on subjects within the scope of reconstructive and plastic surgery, as well as demonstrations of plastic operations. Further information concerning the congress, including the rates which are available for the voyage and for the stay in Paris, may be obtained from the secretariat of the congress, Maison de Chirurgie, 49 Rue de Turin, Paris 8e, France.

Congrès Français d'Urologie—The thirty-ninth Congrès Français d'Urologie will be held in Paris from October 9 to 13. The subject for discussion will be the results of nephrectomy for cancer of the kidney in adults. Further information may be obtained from the general secretary of the Association Française d'Urologie, Dr Louis Michon, 40 Rue Barbet-de-Jouy, Paris, 7e, France.

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PRIMARY CARCINOMA OF THE MALE URETHRA

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Since Hutchinson, in 1861, reported the first authentic case of primary carcinoma of the male urethra, no article on this subject has appeared in which the author personally reviewed all the preceding cases. In most instances the reports made by previous writers have been accepted without consulting the original sources. No doubt one of the reasons this has not been done is the fact that it is not always possible to obtain the original articles.

We have searched the entire literature and, except for a few papers, have been able to abstract the originals. As a result of our work, 32 additional cases have come to light which had not been mentioned in the literature since their publication. The total number of cases reported in the literature is 148 (see table).

LOCATION OF LESION

Carcinoma may occur in any of the anatomic divisions of the urethra. For clinical purposes we have listed the growths in two main groups according to their location. In the first group are those occurring in the anterior, or penile, portion of the urethra, and in the second are those found in the bulbomembranous or posterior portion. Anatomically the bulbous portion is not a part of the posterior portion of the urethra, but it has been included because the symptoms and physical signs of tumors in this location are the same as those of growths occurring in the prostatic and membranous portions. In 65 patients the growth was in the anterior portion of the urethra, in 77 it was in the posterior portion. It is interesting to note that there is little difference in the incidence of carcinoma in the two portions of the urethra.

ETIOLOGIC FACTORS

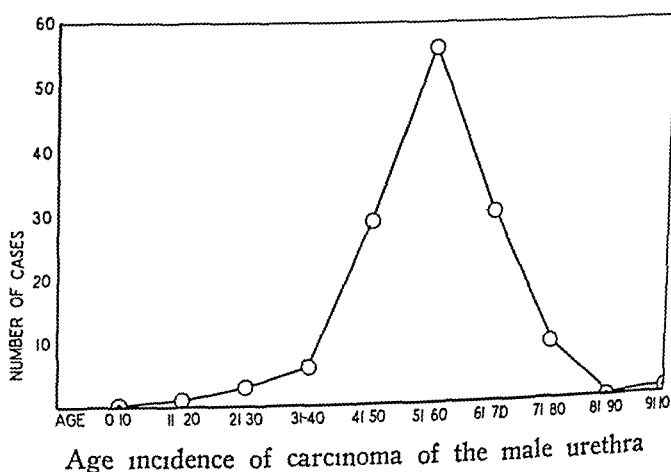
Urethral irritation evidently plays a part in the development of malignant tumor. The presence or absence of stricture was mentioned in 92

From the Department of Urology, the Mount Zion Hospital.

cases, in 76 per cent there was a positive history of this condition. In 7 the structure was traumatic, and in 1 it was congenital. In Kretschmer's case the irritation was chemical, following the injection of Hartzell's solution¹ into the urethra. In 2 patients the growth was an adenocarcinoma, and the question arises whether one should consider such a tumor a true primary carcinoma of the urethra or analogous to the type of growth which develops originally in Cowper's gland and later involves the urethra.

AGE INCIDENCE

Carcinoma of the urethra may occur at any age, although the incidence (see chart) was highest in the fifth decade (56 patients). The youngest patient (Paton's) was 18 years old. Kroiss reported the case of the oldest patient, a man 91 years of age.



PATHOLOGIC PICTURE

In many cases no pathologic report of the growth was made. The following list is a summary of the tumors which were examined, showing the types and incidence of each.

Squamous cell carcinoma	101 cases
or Epithelioma	6 cases
Papillary carcinoma	3 cases
Transitional cell carcinoma	2 cases
Adenocarcinoma	2 cases
Mucoid gland carcinoma	1 case
Columnar cell carcinoma	1 case
Endothelioma	

¹ Hartzell's solution is made up as follows: iodine crystals, 50 grains (3.2 Gm), zinc iodide, 15 grains (0.96 Gm), potassium iodide, 15 grains (0.96 Gm), water, $\frac{1}{2}$ ounce (15 cc), and glycerin, $\frac{1}{2}$ ounce (15 cc).

Watson, Lewis and Selvaggi reported cases in which the growth was limited to the prostatic portion of the urethra. Watson described the tumor in his case as an "irregular, lumpy growth arising from the floor and lateral walls of the urethra with excessive bleeding."

In most cases carcinoma of the posterior portion of the urethra presents itself as an abscess about the size of a walnut in the perineal region, elongated in the anteroposterior diameter. It is located in the median raphe, about 2 cm posterior to the penoscrotal angle. This abscess, which appears as a small tumor-like mass, is tender and red. It discharges thick purulent material through a pinpoint opening. The abscess may heal completely for a time after treatment. It may recur, or it may never heal and may present infiltrated, indurated edges, with a few drops of urine appearing because of the fistulous connection.

The description of Bobbio's case is typical of the sequence of pathologic changes which occur when the posterior portion of the urethra is involved. At the first operation, incision of a perineal abscess was performed, healing was poor, with periurethral infiltration. A second operation was performed, with excision of the abscess together with the infiltrated periurethral tissue. Healing took place for a few weeks, after which the patient was readmitted to the hospital with a perineal fistula. After closure of the fistula the tumor reappeared. It was described as hard and painful. It was the size of an orange, with a shiny, dark bluish adherent skin. Where the skin was missing there were red cyanotic vegetations, in some places these were the size of peas. There were numerous small openings representing fistulous tracts. Incision of this mass revealed a cauliflower-like growth made up of large vegetations with a crater-like ulceration in the center. The skin at the periphery of the growth was cyanotic and at several points was stretched to the point of breaking. On section of the urethra there was observed infiltration into the corpora cavernosa, with complete ulceration of the bulbous portion of the urethra, so that it could not be distinguished from the surrounding neoplastic tissue.

In the anterior portion of the urethra one finds a nodule on the ventral surface of the penis, with or without one or more fistulous tracts. If the growth is at the fossa navicularis there may be an ulceration of the glans with a small pinpoint opening of the urinary meatus.

METASTASIS

Metastasis may occur via either the blood or the lymph channels. In the majority of the cases reported there was no mention of changes in the superficial inguinal glands. It is impossible, therefore, to summarize the incidence of involvement of these glands.

The drainage of the greater portion of the penile part of the urethra is to the deep sublingual glands, that from the bulbomembranous portion, to the external iliac and hypogastric glands and from there to the

common iliac nodes. In some cases in which the inguinal glands were reported to be enlarged, later pathologic examination showed no malignant tissue but merely chronic adenitis. The size of the inguinal glands, therefore, is not a criterion of the pathologic process. The only metastasis in our second case was found in the lung. Metastasis to the scrotum or its contents is rare. We have been able to find only 1 case in which this occurred, that of Geissler, in which the epididymis was involved.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The possibility of carcinoma of the urethra should be considered in the case of a man over 40 who with no previous history of stricture has the symptoms characteristic of this condition. Progressive difficulty of urination is an outstanding symptom. Hematuria occurs infrequently—as a rule, only after instrumentation.

With carcinoma of the posterior portion of the urethra there is usually some progressive urinary difficulty, such as burning, frequent voiding or diminution in the size of the stream. Associated with these symptoms there may appear a soft, fluctuant periurethral mass. Incision of this mass gives only temporary relief. Healing does not take place, subsequent induration of the edges of the wound develops, and sloughing with suppuration occurs. Failure of any periurethral abscess to heal promptly should make one suspect malignant change.

In the anterior portion of the urethra the symptoms are the same. The fact that the patient himself feels a small mass in the penile segment of the urethra and consults a physician early is one of the reasons that the incidence of cures is largest when this is the region involved. If the growth involves the fossa navicularis, an ulcer, with or without a urinary fistula, may exist.

The final diagnosis must depend on urethroscopic examination. Polypoid tissue should be removed for biopsy. One must differentiate this condition from traumatic rupture of the urethra and also from simple stricture. A complete history together with a thorough urethroscopic and physical examination will rule out these conditions.

TREATMENT

Anterior Portion of the Urethra.—In 65 of the 148 cases studied the carcinoma occurred in the anterior portion of the urethra. Various methods of treatment were used, such as (1) partial or complete amputation of the penis, (2) total or partial emasculation, (3) roentgen treatment of the inguinal glands, (4) application of radium to the growth, (5) resection of the urethra and the growth, (6) external urethrotomy and (7) inguinal adenectomy in conjunction with one of the aforementioned forms of treatment.

Amputation of the penis, either complete or partial, was the treatment most often used. It was performed on 35 patients, resulting in 30 recoveries and only 5 deaths. Radium or roentgen therapy without surgical intervention was used for 3 patients, 2 of whom were cured.

When the growth is limited to the distal anterior portion of the urethra, that is, to the part in the region of the glans penis, partial amputation can be safely employed. If, however, the malignant process is in the shaft of the penis, near the bulb, and particularly if the corpora cavernosa are involved, it is best to perform radical amputation.

Emasculation is a needless operation and should never be done, as the testicles are not invaded metastatically. Infiltration of the scrotum with urine, due to rupture of the urethra, has been reported. This may have led some surgeons to perform total emasculation.

It is surprising to note that of the 65 patients in whom the anterior portion of the urethra was involved 35, or 54 per cent, recovered, 19, or 29 per cent died, and in 11 cases or 17 per cent, there was no mention of the end result.

Posterior Portion of the Urethra—Seventy-seven patients had carcinoma of the posterior portion of the urethra, the growth was found most often in the bulbous or the membranous part but occasionally in the prostatic part. A study of the case histories showed many varied forms of treatment. Some, no doubt, were merely palliative, as the disease was too far advanced to permit constructive surgical intervention.

The different forms of treatment described are (1) suprapubic cystostomy, (2) internal urethrotomy, external urethrotomy or both, (3) incision and drainage of the perineum, (4) resection of the urethra and the growth, (5) fulguration and application of radium, (6) excision of the inguinal or of the deep femoral glands, (7) total emasculation, (8) passage of sounds and (9) use of an indwelling catheter.

In this series of 77 patients only 10, or 13 per cent, recovered, while 58, or 75 per cent, died. In 9 cases, or 12 per cent, there was no mention of the end result.

The operation which gave the greatest number of cures was resection of the urethra including the growth. This was performed in 6 of the 10 cases. In 2 of the 6 the inguinal glands also were removed, in a third the penis was amputated and in a fourth radium was applied postoperatively.

In contrast to the gratifying end results obtained in the treatment of growths involving the anterior portion of the urethra carcinoma of the posterior portion presents a gloomy picture. This is no doubt due to the fact that there are no characteristic symptoms of this disease. The patients are treated for stricture and its complications such as rupture of the urethra, periurethral abscess or urinary fistula. By the time the true condition is recognized the growth has become inoperable.

Male Urethra

Summary of One Hundred and Forty-Eight Cases of Carcinoma of the Male Urethra

Author	Age of Patient, Years	Complaints	Gonorrhea	Stricture	Location of Lesion	Treatment	Type of Growth	End Result
Hutchinson	22	Swelling and induration of penis	NM	No	AU	Amputation of penis	Epithelial carcinoma	Cure
Billroth	50	Difficulty of urination, urinary retention	NM	NM	AU	None	No microscopic study	Death
Thiersch	60	Swelling in perineum difficulty on urination incontinence multiple fistulas in right buttock	NM	NM	MU	Tumor removed from meatus External urethrotomy	Epithelial carcinoma	Death
Mears	40	NM	NM	Yes	AU	Refused treatment	Squamous cell carcinoma	NM
Schustler	72	Fever difficulty of urination swelling of penis and scrotum multiple	NM	Yes	BU	Passage of sounds urethroscopy	Squamous cell carcinoma	Death
Poncet	56	Difficulty of urination fistulas difficulty of urination hematuria urinary retention	NM	NM	BU	Internal urethrotomy External urethrotomy	Squamous cell carcinoma	NM
Grünfeld	59	Difficulty of urination multiple	Yes	Yes	BM	Amputation of penis	Epithelial carcinoma	Death
Guyon and Gular	60	Difficulty of urination perineal abscess	Yes	Yes	BMU	Drainage of abscess, division of stricture	Carcinoma	Death
Guyon and Gular	68	Perineal abscess swollen penis	NM	NM	BU	Excision of urethra Wide incisions	Carcinoma	Death
Trebleky	54	Abscess of perineum peri	NM	Yes	BMU	External urethrotomy	Squamous cell carcinoma	Death
Paul	55	Infiltration of perineum perineal	Yes	Yes	BU and AU MU	External urethrotomy	Carcinoma	Death
Albert	60	Perineal abscess Infiltration of urine	No	No	BMU	External urethrotomy	Epithelioma	Discharge in 3 months inguinal glands enlarging
Poncet	70	Difficult and painful urination perineal	No	No	BU	Wide incisions	Squamous cell carcinoma	Death
Griffith	48	Difficulty of urination perineal	Yes	Yes	BMU	Wide incisions	Squamous cell carcinoma	Death
Witzelhausen	53	Inguinal, perineal and scrotal fistulas	Yes	Yes	BU	External urethrotomy	Epithelioma Squamous cell carcinoma	Discharge in 3 months inguinal glands enlarging
Witzelhausen	62	Difficulty of urination swelling in perineum	NM	NM	BMU	External urethrotomy	Squamous cell carcinoma	Death
Dech	56	Bloody discharge from urethra	No	No	AU	Excision of penis	Epithelioma Squamous cell carcinoma	Cure
Parante Chikander	72	Swelling in bulbous region	No	No	AU	Excision of penis	Squamous cell carcinoma	Death
43	43	Fistulas at base of penis	No	No	AU	Excision of urethra to external sphincter (inguinal glands also removed)	Squamous cell carcinoma	Death

Symonds	48	Hematuria, dysuria, frequency tumor above pubes	NM	NM	Entire urethra, including bladder AU	Perineal cystostomy	Epithelioma	Death
Lowenthal	48	Perineal fistulas difficulty of urination	No	Yes (traumatic)	BU	None	Carcinoma	Death
Lowenthal	63	Swelling of perineum and scrotum with fistulas difficulty of urination	NM	NM	BU	Amputation of penis	Carcinoma	Death
Miller		Retention of urine urinary fistula	NM	NM	AU	NM	Cancer	Death
Cabot	1	Painful swelling in perineum perineal fistulas	Yes	NM	BU	Incision and exploration of perineal abscess	Cancer	Death
Buday	67	Difficulty in urination fistulas in penile urethra	No	No	AU	Amputation of two thirds of penis	Cystopapillary cancer	NM
Cheverenu	62	Dysuria urinary fistula tumor in base of scrotum	Yes	Yes	MU	Total emasculation	Epithelioma	Cure
Binzy and Carey	62	Tumefaction and fistula difficulty and pain on urination	Yes	NM	Perineal caver, no, AU	Total emasculation	Epithelioma	Cure
Wassermann	49	Perineal abscess cystitis	Yes	Yes	MU	Internal urethrotomy	Squamous cell carcinoma	Death
Wassermann	67	Urinary infiltration of scrotum and penis	Yes	Yes	MU	Internal urethrotomy	Epithelioma	Death
Wassermann	53	Urinary infiltration	Yes	Yes	BU	Incision and dilatation, resection	Epithelioma	Death
Wassermann	68	Difficulty of urination perineal infiltration	NM	Yes	BMU	Incision	Epithelioma	Death
Hottelinger	55	Dysuria urethral discharge	NM	NM	AU	Amputation of penis	Squamous cell carcinoma	Cure
Hottelinger	53	Urethral discharge difficulty of urination urinary fistula	NM	NM	AU	Amputation of penis	Carcinoma	Death
Van Hook	73	Bleeding from meatus swelling and abscess posterior to glans penis	No	NM	AU	Amputation of penis removal of inguinal glands	Carcinoma	Death
Boase	23	Difficulty of urination retention urinary extravasation through perineum	Yes	Yes	BU	External urethrotomy cystostomy external urethroostomy	Epithelioma	Death
Bisland and Chavannaz	54	Difficulty of urination dribbling pain in penis	Yes	Yes	AU	Amputation of two thirds of penis removal of inguinal glands	Epithelioma	Death
Scott	54	Difficulty of urination swelling in perineum enlarging and ulcerating, inguinal glands	No	NM	BU	Perineal incision	Squamous cell carcinoma	Cure
Montgomery	54	Bloody urethral discharge	Yes	Yes	AU	Perineal urethrotomy	Carcinoma with an unquestionable mucoid type of epithelium	Death
Gayel	70	Swelling of penis difficulty of urination hematuria	NM	?	AU	Amputation of penis	Epithelioma	Cure
Moresth	73	Yesion at meatus dysuria	NM	NM	AU	None	Carcinoma (clinically)	NM

In this table the following abbreviations are used: BU, bulbous portion of urethra; MU, membranous portion of urethra; AU, anterior portion of urethra; BU, bulbomembranous portion of urethra; MU, membranous portion of urethra; AU, anterior portion of urethra; BU, bulbomembranous portion of urethra; MU, membranous portion of urethra; AU, anterior portion of urethra.

Summary of One Hundred and Forty-Eight Cases of Carcinoma of the Male Urethra—Continued

Author	Age of Patient, Years	Complaints	Gonorrhea	Stricture	Location of Lesion	Treatment	Type of Growth	End Result
Morestin	47	Ulceration at meatus dysuria painful erections of micturition, perineal swelling	NM	NM	AU	Amputation of half of penis	Epithelioma	Cure
Lipman Wulf	50	Dysuria perineal swelling	NM	Yes (traumatic)	PU	Incision and drainage of perineum, removal of tissue	Epithelioma cell carcinoma	Death
Bobbio	53	Acute retention, perineal swelling, fistula	Yes	Yes	BU	Excision of fistula and granulation tissue	Epithelioma cell carcinoma	Death
Ivannant	48	Perineal swelling, with fistula	Yes	Yes	BMU	Incision and drainage	Carcinoma (flat cellular)	Death
Burkhardt	59	Difficulty of urination	Yes	Yes	15 cm from meatus	NM	Carcinoma	NM
Burkhardt	54	Difficulty of urination	Yes	Yes	12 cm from meatus	NM	Carcinoma	Death
Hall	49	Perineal abscesses and fistulas	NM	NM	BU	Incision of abscess excision of growth	Squamous cell carcinoma	NM
Wood	48	Chronic retention swelling in the perineum	NM	NM	AU	Incision of abscess	Squamous cell carcinoma	Cure
Montgomery (personal communication to Hall)	53	Dysuria circular ulceration at surface of meatus infiltration of glans penis	NM	NM	AU	Amputation of penis	Squamous cell carcinoma	Cure
Shattock	51	Hematuria dysuria narrowing of urethra	No	NM	NM	1903, removal of ulcer and roentgen treatment 1905, amputation of penis	Squamous cell carcinoma	NM
Platt	59	Difficulty of urination urinary fistula and fever perineal swell	NM	NM	AU	Amputation of anterior portion of penis	Epithelioma	Cure
Rupke	46	Chills and fever perineal swelling fistulas	No	NM	NM	Amputation of penis	Squamous cell carcinoma	Death
Rupke	38	Dysuria hematuria weak urinary stream	No	Yes (congenital)	BMU	External urethrotomy	Squamous cell carcinoma	Death
Prothman	53	Difficulty of urination induration in perineum	Yes	Yes	BMU	External urethrotomy	Squamous cell carcinoma	Death
Prothman	61	Chills and fever dysuria weak stream pain at base of penis	Yes	Yes	MU	Excision of growth external urethrotomy, amputation of penis	Carcinoma	Death
Prothman	59	No urinary symptoms	?	NM	AU	Perineal incision and drainage	Squamous cell carcinoma	Cure
Prothman	62	Acute retention	No	Multiple	BU	Perineal section	Epithelioma	Death
Prothman	57	Abscess in perineum difficulty of urination infected ulceration near meatus	Yes	Yes	BMU	Indwelling catheter	Epithelioma	NM
Prothman	57	Acute retention	Yes	Yes	AU	Amputation of inguinal glands	Epithelioma	Cure

Author	Age of Patient, Years	Complaints	Gonorrhea	Stricture	Location of Lesion	Treatment	Type of Growth	End Result
Muller	53	Nodules along penile urethra	Yes	Yes	AU	Internal urethrotomy, resection of 4 cm of urethra	Carcinoma	Death
Rizzi	49	Growth extending from meatus	Yes	Yes	AU (spread to bulbous urethra)	Removal of penis and portion of men urethra	Squamous cell carcinoma	NM
Onlei	64	Difficult and painful urination, perineal mass acute retention	Yes	Yes	Yes	Suprapubic cystostomy, perineal incision	Epidermoid carcinoma	Death
Onlei	51	Pain in penis on pressure, difficulty in starting stream, pain and fistula in perineum	Yes	Yes	Yes	Incision and curettage of abscess walls	Epithelioma	Death
Imbert	NM	Difficulty of urination, perineal infiltration	NM	Yes	AU (from bladder to scrotum)	Incision of abscess walls	NM	NM
Scholl and Bransch	48	Swelling of perineum, symptoms of stricture	Yes	Yes	NM	Passage of sounds	Squamous cell carcinoma	Cure
Culver and Forster	53	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	Yes	Excision of growth, reconstruction of urethra	Squamous cell carcinoma	Cure
Kretschmer	56	Swelling of penis, difficulty of urination	Yes	Yes	Yes	Excision of growth, reconstruction of urethra	Papillary carcinoma	Cure
Uchida	52	Swelling of penis, difficulty of urination	NM	NM	NM	Amputation of penis, excision of inguinal glands	Papillary carcinoma	Death
Laurie	71	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Carcinoma	Death
Palme	55	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Squamous cell carcinoma	Death
Laton	57	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Squamous cell carcinoma	Death
Dahl	58	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Squamous cell carcinoma	Death
Christen	60	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Squamous cell carcinoma	Death
105	60	Swelling of penis, induration and tenderness of shaft of penis, with fistula formation	NM	NM	NM	Amputation of penis, excision of inguinal glands	Squamous cell carcinoma	Death

Young, and Davis	38	Acute retention perineal and scrotal tumefaction perineal fistula	NM	Yes, traumatic	MU	Incision of abscesses perineal urethrotomy	Squamous cell carcinoma	Death
Young, and Davis	40	Chills and fever perineal abscesses and fistulas	NM	NM	MU	Incision of abscesses	Squamous cell carcinoma	Death
McCune	47	Difficulty of urination acute retention	Yes	Yes	BU	Urethral dilatation roentgen therapy suprapubic cystostomy	1 pidermold carcinoma	NM
Lukal Yoshida	50	Dysuria weak stream	No	No	AU	Amputation of penis	Carcinoma	Cure
Wurnsler	37	Perineal swelling, later abscess and fistula formation	Yes	NM	BMU	Excision of perineal fistula incision of abscess	1 pithelloma	Cure Death
Marion	42	Urinary abscess and fistula	NM	NM	BMU	Operation of abscesses radium therapy	1 pithelloma	Death
Marion	40	Pain in bulbous region	NM	NM	BU	Cystostomy resection by circular urethrorrhaphy	1 pithelloma	Death
Deros	NM	NM	NM	NM	NM	Internal urethrotomy perineal incision	1 pithelloma	Death
Robb	69	Acute retention indurated mass in perineum enlargement of both testes	No	NM	BU	Amputation of penis splitting of scrotum	1 transitional cell carcinoma	Death
Robb	59	Small hard nodule at peno scrotal junction palpable mass in bulbous urethra	Yes	Yes (instrumented 177 times)	BMU	Complete amputation	1 transitional cell carcinoma	Death
Hieberbach and Peters	42	Difficulty of urination acute retention	NM	Yes (traumatic)	BMU	Perineal incision and drainage	1 pidermold carcinoma	Death
Hieberbach and Peters	61	Pain and blood in urine urinary fistula	Yes	Yes	MPU	Incision and drainage of perineum application of radium	1 pidermold carcinoma	Death
Arifoglio	52	Difficulty of urination swelling of perineum	Yes	No	BMU	Radium suprapubic cystostomy	Squamous cell carcinoma	Death
Watson	0	Hematuria difficulty in starting stream	Yes	NM	PU (prostatic)	Suprapubic cystostomy diathermy incision		
Watson	71	Sensation of obstruction near meatus	Yes	Yes	AU (fossa navicularis)	Excision of radium roentgen therapy	Mucous membrane epithelioma	Cure
Langley	42	Periurethral abscess near clitoris urethral induration to penoscrotal junction	?	?	AU	Amputation of penis excision of inguinal glands	Squamous cell carcinoma	Cure
Flamm	70	Hemorrhage from meatus growth protruding from meatus	Yes	No	AU	Amputation of penis after radium application	Squamous cell epithelioma	Cure
Huggins and Curtis	79	Mass in perineum	Yes	Yes	AU	Amputation of penis	Squamous cell carcinoma	Cure
Belma	57	Dysuria	No	No	AU	Excision of urethra roentgen rays to inguinal glands and perineum	Adenocarcinoma	Cure

Summary of One Hundred and Forty-Eight Cases of Carcinoma of the Male Urethra—Continued

Author	Age of Patient, Years	Complaints	Gonorrhea	Stricture	Location of Lesion	Treatment	Type of Growth	End Result
Gelsler	64	Perineal fistula	NM	NM	MU, PU	External urethrotomy	Epithelial carcinoma	Death
Lower	58	Acute retention	No	Yes	MU	Suprapubic cystostomy, resection of urethra	Squamous cell carcinoma	Cure
	42	Acute retention	Yes	Yes	MU	Suprapubic puncture, resection of urethra	Papillary carcinoma	Cure
Lower	61	Difficulty of urination	Yes	Yes	Indurated area in perineum	Suprapubic cystostomy, resection of urethra	Adenocarcinoma	Death 1 year later
Beck	64	Weakness of urinary stream	Yes	Yes	Indurated area in perineum	Suprapubic cystostomy, resection of urethra	Squamous cell carcinoma	Cure
Sokolov	59	Difficulty of urination	Yes	No	AU	Resection of inguinal glands	Mucoid glandular carcinoma	No metastasis recurrence 4 months later
Kirwin	62	Acute retention	Yes	NM	AU	Removal of inguinal glands removed by growth inguinal masses dissected, radon seeds	Epithelioma	NM
	64	Ulcer at meatus	Yes	Yes	NM	Partial amputation of penis	Squamous cell carcinoma	Cure
	60	Bloody discharge from meatus	Yes	Yes	NM	Amputation of penis	Squamous cell carcinoma	Death
Boggon	53	Indurated area in penis	Yes	Yes	NM	Amputation of deep inguinal and deep glands excised	Squamous cell carcinoma	Cure
LaZarus	62	Frequency of urination	Yes	Yes	Yes	Incision and drainage of perineum external urethrotomy	Squamous cell carcinoma	Death
McNally	71	Painful and difficult urination	Yes	NM	NM	Suprapubic cystostomy	Transitional cell carcinoma	Cure
Astrand	66	Pain on urination	Yes	No	Yes	Incision and drainage of abscess in cavernosa	Squamous cell carcinoma	Death
Coldstein and Alteshouse	60	Pain on urination	Yes	No	Yes	Suprapubic cystostomy radical resection including lymphatics	No sections made	Death
Chute	60	Swelling of urethra	Yes	NM	Yes	Complete emasculation	Carcinoma	Death
Chute	60	Swelling of urethra	Yes	NM	Yes	Inoperable		
Chute	60	Swelling of urethra	Yes	NM	Yes	Inoperable		

Author	Case	History	Sex	Age	Operation	Result	Death
König	49	Difficulty of urination, chills and fever, urinary infiltration with fistula	Yes	MU	Excision of mass, amputation of penis	1 pithelloma	Death
Shankel	52	Urinary retention, tumefaction to perineal urethra, acute pain to perineum, ulceration and fistula, fetid purulent discharge	Yes	PU	Urethral catheter (in dwelling) later, total emasculation	1 pithelloma	NM
Devere	50	Urinary retention, swelling and urinary infiltration of perineum	Yes	BU	Internal urethrotomy, removal of growth, amputation of penis one month later	1 pithelloma	Cure
Meurer	59	Painful urination, perineal tumefaction	Yes	BU	Internal urethrotomy, incision of perineum, radium	1 pithelloma	NM
Dohrmanbeck	59	Difficulty of urination, painful urination	No	AU	Amputation of one third of penis, incision of glands removed	1 endothelloma or, from lining, from blood vessels	Cure
Mortenson	61	Acute retention, difficulty in voiding, stream dribbling, perineal abscess	NM	AU	Incision of abscess, suprapubic cystostomy	Squamous cell carcinoma	Death
McLard	51	Incontinence, bloody discharge, dysuria	No	BU	Amputation of penis plus suprapubic cystostomy, inguinal adenectomy later, roentgen therapy	Squamous cell carcinoma	Cure
Miller	58	Narrowing, stream dysuria	No	AU	Palliative	Carcinoma of urethra	Death
Smith	63	Tumor in penis, moderate enlargement of distal third, papillary growth on separate edges of urethra	NM	AU	Biopsy, total amputation of penis, excision of inguinal and iliofemoral nodes, transplant of urethra to perineum	Epithelioma	Cure
Smith	64	Painful swelling of perineum, chills and fever	NM	BU	Incision of abscess, suprapubic cystostomy, palliative therapy	Squamous cell carcinoma	Death
Twiss	67	Swelling on ventral surface of penis, urinary fistula, hematuria and dysuria	NM	AU	Mentotomy and sounds, suprapubic cystostomy, palliative therapy	Squamous cell carcinoma	Cure
Twiss	63	Painful urination, difficult dilatation of strictured urethra, loss of weight	Yes	PU	Cystostomy, radium, urethral transplant	Papillary carcinoma	NM
Crumpacker	69	Hygienic near mentus on labia, posteriorly (improved under anti-phlogistic therapy)	Yes	AU	Partial amputation of penis	1 lat cell carcinoma	NM
Harbach	67	Swelling of penis, hematuria, pyuria, perineal abscess, urinary fistula	Yes	AU	Incision and drainage, partial amputation of penis, inguinal adenectomy	Squamous cell carcinoma	Cure
Townsend and Muleady	70	Swelling of perineum, terminal hematuria, difficult dilatation of urethra	Yes	BU	Roentgen therapy	1 pithelloma carcinoma	Death
Putzmann and Colloff	72	Weak stream, frequent dilatations, perineal abscess following biopsy	Yes	AU	Cystostomy, incision, abscess, ureteral transplant (2 stage)	1 pithelloma carcinoma	Died
Kratmann and Colloff	71	Weakness of urinary stream, pain and swelling at base of penis, later perineal fistula	Yes	PU	Internal urethrotomy, suprapubic cystostomy, incision, inguinal abscess, biopsy, urethral growth	Squamous cell carcinoma	Died

In reviewing the entire series of 148 cases, we were interested to note that inguinal glands had been removed in only 20 cases, 16 of anterior and 4 of posterior urethral involvement. Of the 45 patients in the entire series who recovered, inguinal adenectomy had been performed on only 13. In several patients the glands were seen on clinical examination to be enlarged. Sections after removal showed inflammatory changes but no metastasis.

Despite the fact that inguinal adenectomy was performed on only approximately 4 per cent of the patients who recovered, surgical intervention should include removal of the inguinal glands in order to obviate the possibility of metastasis by way of the lymphatics. Huggins and Curtis described the surgical procedure in detail, and repetition at this time is needless.

SUMMARY AND CONCLUSIONS

Primary carcinoma of the male urethra is a rare disease, only 148 cases having been previously reported. Of the total number of growths, 65 originated in the anterior and 77 in the posterior portion of the urethra. In 6 cases the location with reference to the site of origin of the growth was not mentioned. Two new cases bring the total to 150.

A thorough search of the literature revealed many cases which have not been mentioned since their original publication.

The greatest incidence of carcinoma of the male urethra is in the fifth decade.

In 88 per cent of the cases in which a pathologic report was made the tumor was a squamous cell carcinoma.

The inguinal glands are rarely involved, and in many cases enlargement is due to infection rather than to metastasis.

The treatment of carcinoma involving the anterior portion of the urethra which has given the greatest number of cures is partial or complete amputation of the penis.

The best results when the malignant process involved the posterior portion were obtained by resection of the urethra with the included growth.

Inguinal adenectomy is advisable in all cases.

Sufficient data have not been obtained up to the present time to enable one to evaluate roentgen and radium treatment without previous surgical intervention.

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PANCREATICOGASTROSTOMY

EXPERIMENTAL TRANSPLANTATION OF THE PANCREAS INTO THE STOMACH

E COOPER PERSON JR, MD

AND

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NEW YORK

HISTORICAL CONSIDERATIONS

The early work of Brunner¹ in 1682, as reported by Ceccherelli, demonstrated that partial extirpation of the pancreas did not impair the health and digestion of the experimental animal. This salient observation has led to the development of surgical procedures which have been successful as long as the main pancreatic and biliary ducts have been left intact. However, investigations concerning the feasibility of attacking the head of the pancreas and thereby excluding the external pancreatic secretion from the intestinal tract have led to conflicting results.

A historical survey of these related experimental problems shows that the conflicts date from early time.

The first experimental approach to this subject was carried out by Bernard². He occluded the pancreatic ducts by injecting them with paraffin and observed a marked disturbance in the absorption of fat from the intestinal tract, with early death of the animal. From this observation he concluded that pancreatic juice is highly essential for digestion. This conclusion was refuted by a number of investigators, namely, Schiff,³ Cohnheim⁴ and Martinotti,⁵ who excluded the pancreatic enzymes from the intestinal tract in various ways and found that digestive functions continued in a satisfactory manner.

From the Department of Surgery of the New York Hospital and the Cornell University Medical College

1 Brunner, C L, cited by Ceccherelli, A. *La chirurgica du pancreas*, Comptes rendus de la Congres internationale de medecin, Paris, 1900, p 159

2 Bernard, C. *Memoire sur le pancreas et sur le role du suc pancreatique dans les phenomenes digestifs, particulierement dans la digestion des matieres grasses neutres*, Paris, J B Bailliere, 1856

3 Schiff, 1862, cited by Oser, in Nothnagel, H. *Encyclopedia of Practical Medicine*, translated by A Stengel, Philadelphia, W B Saunders Company, 1902

4 Cohnheim, J, 1882, cited by Senn⁶

5 Martinotti, G. *Sulla estirpazione del pancreas*, Giornale Accademia di Torino 36 348, 1888

The extensive and enlightening studies of Senn⁶ demonstrated that the pancreas could be subjected to direct surgical procedures. He concluded, however, that complete resection of the head of the pancreas with the common duct is not justifiable and that procedures on this portion of the gland should be limited to partial excision with preservation of the common duct, he further accentuated his opinion by stating that if disease develops in this region it "precludes the propriety of operation." However, Nemier⁷ presented a review of clinical surgical treatment of the pancreas and concluded that radical intervention for malignant lesions of this organ is surgically feasible. He referred to the need of establishing a communication between the pancreas and the intestine and cited Codivilla's case in which this procedure was carried out successfully.

Nemier's review and the further observation that pancreatectomy is followed by enormous loss of fat and nitrogen in the stools (Abelmann⁸, de Dominicis⁹, Sandmeyer¹⁰) probably led Biondi¹¹ to perform an experimental investigation with the purpose of establishing a new exit for the external secretion of the pancreas. Biondi implanted the transected portion of the pancreas and duct of Wirsung into the duodenum, but was unsuccessful. The 6 dogs which he subjected to this procedure died of peritonitis and gangrene of the small intestine. Similar results were obtained by Ceccherelli, who used 2 dogs. Both experimentalists concluded that the theory of pancreatic transplant is tenable but the procedure technically not feasible.

In an attempt to clarify the diverse conclusions reached regarding the effects of excluding the pancreatic enzymes, Lombroso¹² in 1908 repeated his work of 1894 (in Minkowski's clinic). He demonstrated that with the external secretions of the pancreas completely excluded the absorption of food is adequate and compatible with life. In con-

6 Senn, N. The Surgery of the Pancreas as Based upon Experiments and Clinical Researches, *Am J M Sc* **92** 141, 1886

7 Nemier, H. Chirurgie de pancreas, *Rev de chir* **13** 618, 757 and 1007, 1893

8 Abelmann, M. Ueber die Ausnutzung der Nahrungsstoffe nach Pankreas-entirpation mit besonderer Berücksichtigung der Lehre von der Fettresorption, *Inaug Dissert*, Dorpat, C Mattiesen, 1890

9 de Dominicis, N. Legatura del dotto di Wirsung, *Rev clin e terap* **16** 60, 1894

10 Sandmeyer, W. Ueber die Folgen der partiellen Pankreasentirpation beim Hunde, *Ztschr f Biol* **13** 12, 1895

11 Biondi, D. Contributo clinico e sperimentale alla chirurgia del pancreas *Clin chir* **4** 131, 1896

12 Lombroso, U. Kann das nicht in den Darm sezernierende Pankreas auf die Nährstoffresorption einwirken? *Arch f exper Path u Pharmakol* **60** 99 1908

tradiction to this, Pratt, Lamson and Marks¹³ proved that animals show a markedly diminished absorption of fat and nitrogen, as evidenced by large residues demonstrated in the stools by careful chemical analysis.

The excellent article by Desjardins¹⁴ on pancreatectomy reintroduced the feasibility of radical operative intervention for carcinoma of the head of the pancreas. For the first time the surgical procedure was designed in accord with the complex physiologic and anatomic character of the gland and with full recognition of the tremendous difficulties encountered in such an approach. Desjardins claimed that the key to radical operations on the pancreas is duodenal resection and restoration of the communication between the pancreas and intestine. He found it essential to restore the continuity of the pancreatic flow in order to avoid the danger of intra-abdominal leakage from the pancreatic stump or the formation of a pancreatic retention cyst. As a result of his thorough investigation, Desjardins offered a two stage procedure for radical removal of a malignant lesion of the head of the pancreas. The two stages consisted in (a) reestablishment of the continuity of the intestinal and biliary tracts and (b) resection of the duodenum and the head of the pancreas and restoration of the flow of pancreatic secretions by pancreaticojejunostomy.

A few months after Desjardins' publication, Sauve¹⁵ presented an article approving the logic of a pancreaticoduodenostomy as a necessary step in radical procedures involving the head of the pancreas. However, he claimed that to reestablish the communication between the pancreas and intestine was ideal but not surgically practical at the time. He provided instead an extra-abdominal outlet for the retained pancreatic secretions by attaching the pancreatic stump to the anterior abdominal wall, thus creating a pancreatic fistula.

In 1909, Coffey¹⁶ reported the first successful experimental transplantation of the pancreas into the jejunum and described the difficult and intricate technic by which it was accomplished. This procedure, which he called "pancreaticoenterostomy," consisted of uniting a loop of jejunum in the form of a U after the manner of a Finney pyloroplasty and implanting the stump of the pancreas into this loop. His technic was complicated and difficult because he assumed that in order to prevent leakage it was necessary to bring the transplanted pancreas into contact with a considerable area of serosal surface. Coffey concluded that pan

13 Pratt, J. H., Lamson, P. D., and Marks, H. K. The Effect of Excluding Pancreatic Juice from the Intestine, *Tr. A. Am. Physicians* **24** 266, 1909.

14 Desjardins, A. Technique de la pancreatectomie, *Rev. de chir.* **1** 945 1907.

15 Sauve, L. Des pancréatectomies et spécialement de la pancreatectomie céphalique, *Rev. de chir.* **37** 113, 1908.

16 Coffey, R. C. Pancreato-Enterostomy and Pancreatectomy, Preliminary Report, *Ann. Surg.* **50** 1238, 1909.

creaticoenterostomy is feasible surgically and that the implanted pancreas in animals showed no pathologic changes up to the time the animals were killed (thirty days). These observations were verified by Sweet and Simons¹⁷ and by Patrie, Pyle and Vale¹⁸ who used a less complicated technic.

Concurrently with these surgical efforts, further problems associated with the exclusion of the external secretion of the pancreas from the intestinal tract were being studied. Fisher¹⁹ and also Allen, Bowie, McLeod and Robinson²⁰ demonstrated the presence of fatty infiltration and degenerative changes of the liver in pancreatectomized animals at death. Hershey and Soskin²¹ (1932) confirmed this work and found that death of the animal could be prevented if the diet included phospholipids, such as lecithin and choline, or raw pancreas. Berg and Zucker²² deprived the dogs of pancreatic enzymes by means of a modified Elman-McCaughon pancreatic fistula and consistently found marked hepatic changes. The authors concluded that the underlying common factor was exclusion of the external secretion from the intestine.

Contradicting results were obtained by Van Prohaska, Dragstedt and Harms²³ on the basis of their experiments which showed that the external secretion of the pancreas played no role in preventing fatty infiltration and degeneration of the liver. They observed that changes in the liver did not occur in dogs provided with total pancreatic fistulas or in dogs with ligated pancreatic ducts and degeneration of the pancreatic parenchyma. They proposed the existence of a new hormone concerned in some manner with the normal transport and utilization of fat²⁴. On the other hand, Ralli, Rubin and Present²⁵ were unable to

17 Sweet, J. E. and Simons, I. H. Some Experiments on the Surgery of the Pancreas. *Ann Surg* **61** 308 1915

18 Patrie, H. H., Pyle, L. A. and Vale, C. F. Recent Experimental Studies on the Pancreas. *Surg Gynec & Obst* **24** 479 1917

19 Fisher, N. F. Attempts to Maintain the Life of Totally Pancreatectomized Dogs Indefinitely by Insulin. *Am J Physiol* **67** 634 1924

20 Allen, F. N., Bowie, I. J., McLeod, I. I. R. and Robinson, W. L. Behavior of Depancreatized Dogs Kept Alive with Insulin. *Brit J Exper Path* **5** 75 1924

21 Hershey, J. M., and Soskin, S. Substitution of "Lecithin" for Raw Pancreas in the Diet of the Depancreatized Dog. *Am J Physiol* **98** 74 1931

22 Berg, B. N., and Zucker, I. F. Liver Changes After Deprivation of External Pancreatic Secretion. *Proc Soc Exper Biol & Med* **29** 68 1931

23 Van Prohaska, J., Dragstedt, L. and Harms, H. P. The Relation of Pancreatic Juice to the Fatty Infiltration and Degeneration of the Liver in the Depancreatized Dog. *Am J Physiol* **117** 166 1936

24 Dragstedt, L. R., Van Prohaska, J. and Harms, H. P. Observations on a Substance in the Pancreas (a Fat Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatized Dog. *Am J Physiol* **117** 175, 1936

support the contention of Dragstedt and his associates concerning a fat-metabolizing hormone produced by the pancreas. They concluded the findings of Dragstedt and his co-workers may have been due to the short period the animals were under observation (four to twelve weeks). Here may be mentioned also the work of Best and Ridout²⁶ and that of MacKay and Barnes²⁷ on rats. These investigators observed that the pancreatic extract described by Dragstedt exercised such lipotropic effects as could be expected from its choline and protein content.

Chaikoff, Connor and Biskind²⁸ were able to keep dogs alive for five years after complete pancreatectomy by feeding a special diet supplemented by insulin. Their extended observations demonstrated a sequence of striking changes in the liver, namely, fatty infiltration, hyaline degeneration and atrophy of the hepatic cells at the periphery of the lobules and fibroblastic proliferation ending with the typical fibrotic lesion of cirrhosis. Boyce and McFetridge²⁹ made an experimental study of the operative procedures which involve exclusion of the pancreatic secretion from the intestinal tract, with special reference to the metabolism of the liver cell. They concluded that when partial pancreatectomy is a necessary part of the operation for malignant disease of the ampulla and periampullary regions, fatty metamorphosis of the liver will occur unless provisions are made to prevent it.

In summarizing this historical survey it may be stated

1 In the surgical treatment of malignant lesions of the pancreas, loss of the pancreatic enzymes should be avoided if a practical means is available to reintroduce them into the intestinal tract.

2 Exclusion of pancreatic secretion from the intestinal tract does not appear seriously to interfere with normal digestion.

3 Marked changes in the liver, such as fatty infiltration and degeneration, occur when the intestinal tract is deprived of pancreatic secretion.

25 Rall, E. P., Rubin, S. H., and Present, C. H. The Liver Lipids and Fecal Excretion of Fat and Nitrogen in Dogs with Ligated Pancreatic Ducts, *Am J Physiol* **122**:43, 1938.

26 Best, C. H., and Ridout, S. H. The Pancreas and the Deposition of Fat in the Liver, *Am J Physiol* **122**: 67, 1938.

27 MacKay, E. M., and Barnes, R. N. Influence of a Pancreas Extract and Other Proteins on Liver Fat and Ketosis, *Proc Soc Exper Biol & Med* **38**: 410, 1938.

28 Chaikoff, I. L., Connor, C. L., and Biskind, G. R. Fatty Infiltration and Cirrhosis of the Liver in Depancreatized Dogs Maintained with Insulin, *Am J Path* **14**: 101, 1938.

29 Boyce, F. F., and McFetridge, E. M. An Experimental Study of Operations Which Involve Exclusion of the Pancreatic Secretion from the Intestinal Tract, with Special Reference to the Possible Effects on Protein and Fat Digestion and on the Metabolism of the Liver Cell, *Surgery* **4**: 51, 1938.

tion over a long period. A dietary safeguard may be found in such substances as lecithin, choline and raw pancreas (or alcoholic extracts of pancreas).

4 It is well to keep in mind Handelsman's³⁰ warning that great care must be given to a study of the literature before accepting or rejecting one observer's opinion concerning the external secretion of the pancreas and the effects of the absence of these enzymes from the intestinal tract.

Malignant lesions of the ampulla of Vater and of the head of the pancreas present a common therapeutic problem both from the anatomic and the physiologic standpoint. Radical operation for lesions affecting these structures seems justified, for without it a fatal outcome is inevitable and usually rapid. However, the effects of radical extirpation on the physiologic function of neighboring organs must be seriously considered. The most important of these adjacent structures are the pancreatic duct and the common duct. In a radical procedure these ducts must be sacrificed, with resulting exclusion of the enzymes of the pancreas and of the bile from the intestinal tract. The opinion that complete deprivation of pancreatic secretion is not detrimental remains open to controversy, therefore it seemed important to study the feasibility of reintroducing this secretion. Were it possible to devise a practical procedure to accomplish this, several purposes would be served.

1 If an outlet for the pancreatic secretion were provided, there is every reason to believe that the pancreas would retain its normal function.

2 It would prevent the fatty infiltration and degenerative changes in the liver which experimental observations lead one to expect after exclusion of the pancreatic secretion from the intestinal tract. These pathologic alterations of the liver interfere with its normal function and increase the danger of intercurrent systemic infection.

3 The external secretion from the pancreas amounts at least to 700 to 800 cc daily. This secretion continues to amount to 200 to 300 cc in spite of the parenchymatous atrophy and fibrosis of the gland associated with partial occlusion of the duct. Surgical attempts to curb this secretion merely by ligation of the duct without providing a suitable outlet are impractical and are likely to lead to pancreatic fistula, pancreatic abscess or hemorrhagic pancreatitis, all serious conditions in an already debilitated patient.

4 As a preliminary step to radical operation it would appear beneficial to reintroduce the pancreatic enzymes into the intestinal tract since

30 Handelsman, M. B. The Digestive and Absorptive Function of the External Secretion of the Pancreas. *Ann Int Med* 11: 1470, 1938.

pancreatic insufficiency seems to be one of the most significant factors in the symptomatology and the rapid terminal course of malignant tumors of this region

Fear of the well known complications acute pancreatitis and peritonitis following operations on the pancreas in man has given this organ the reputation of a surgical "noli me tangere" Judd and Hoerner³¹ enumerated other factors which have retarded progress in surgical treatment of the pancreas, such as the generally poor condition of the patient, the insidious onset of the disease, the relative inaccessibility of the lesions the intimate relation to major abdominal structures which cannot be sacrificed and the extreme technical difficulties of any surgical procedure in this region Yet efforts to create a new outlet for the secretions of the pancreas have not been abandoned

PURPOSE, METHOD AND RESULTS OF THE EXPERIMENTAL STUDY

The first successful transplant of the pancreas into the stomach was carried out by Tripodi and Sherwin³² in 1934 Prior to that operation the small intestine usually had been selected as the site for the implant, but Tripodi and Sherwin chose the stomach because of its greater accessibility and size and in order to prevent obstruction of the lumen of the bowels and strangulation of the transplanted pancreas In addition, the acid content of the stomach reduces but does not completely destroy the activity of the pancreatic enzymes, thus decreasing the potential danger of pancreatitis These investigators gave a detailed account of the technic by which the pancreatic stump was transplanted into the posterior wall of the stomach through a triradiate incision with invaginated serosal surfaces

Because this was a blind method of transplantation, experimental work was undertaken to find a means by which the operation could be accomplished under direct vision

When the problem was approached in experimental animals, it was realized that there are minor but significant anatomic variations between the human and the canine pancreas³³ The most important of these is the presence in the dog of a protective peritoneal covering over the organ, the absence of which in the human being subjects him to greater danger of spreading infection To simulate as nearly as possible the condition found in man, this protective peritoneal covering can be stripped off the pancreas in dogs

31 Judd, E. S., and Hoerner, M. T. Surgical Treatment of Carcinoma of the Head of the Pancreas and of the Ampulla of Vater, *Arch Surg* 31 937 (Dec) 1935

32 Tripodi, A. M., and Sherwin, C. F. Experimental Transplantation of the Pancreas into the Stomach, *Arch Surg* 28 345 (Feb) 1934

33 Bradley, O. C. Topographical Anatomy of the Dog, New York The Macmillan Company, 1927

Technic—The peritoneal cavity was opened through an upper right rectus incision, and the first portion of the duodenum and the attached pancreas were delivered. The main and accessory ducts and their entrance into the duodenum were exposed by carefully freeing the duodenum from the adherent pancreatic tissue. The main pancreatic duct, which corresponds to the duct of Santorini in man, was doubly ligated and divided. Stay sutures of arterial silk were placed in the lateral walls of the remaining accessory duct (duct of Wirsung), and it was divided (fig 1). These sutures afforded a means of traction, so that the organ could be manipulated without traumatizing the friable pancreatic tissue.

The pancreas was then transected just distal to the accessory duct. (This division must be carried out with care in order to identify the central duct and to control bleeding from the pancreaticoduodenal vessels which traverse the superior border of the gland.) The stump of the pancreas, consisting of the neck and

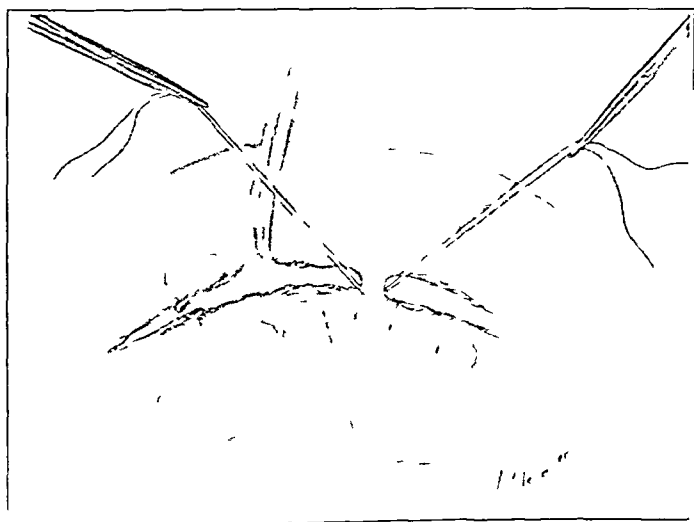


Fig 1—Exposure of the main and accessory ducts and their entrance into the duodenum. The ducts are exposed by carefully freeing the duodenum from the adherent pancreatic tissue. The dotted lines indicate transection of the pancreas.

body and the ducts, was implanted into the stomach under direct vision in this manner (fig 2).

A longitudinal incision was made in the anterior wall of the stomach midway between the greater and lesser curvatures and close to the pylorus (fig 3). With a finger in this opening to direct further procedures the stomach was rotated so that a transverse incision might be made in the posterior wall opposite the first opening (fig 3). This was approximately 2 cm in length and lay near the pylorus.

Silk stay sutures were passed through each side of the stump of the pancreas at a point 1 cm from the transected end care being taken to avoid puncturing the pancreatic duct or vessel. These stay sutures were brought into the stomach through the posterior stoma threaded into needles and returned to the outside by passing through the entire thickness of the gastric wall at a point 1 cm from

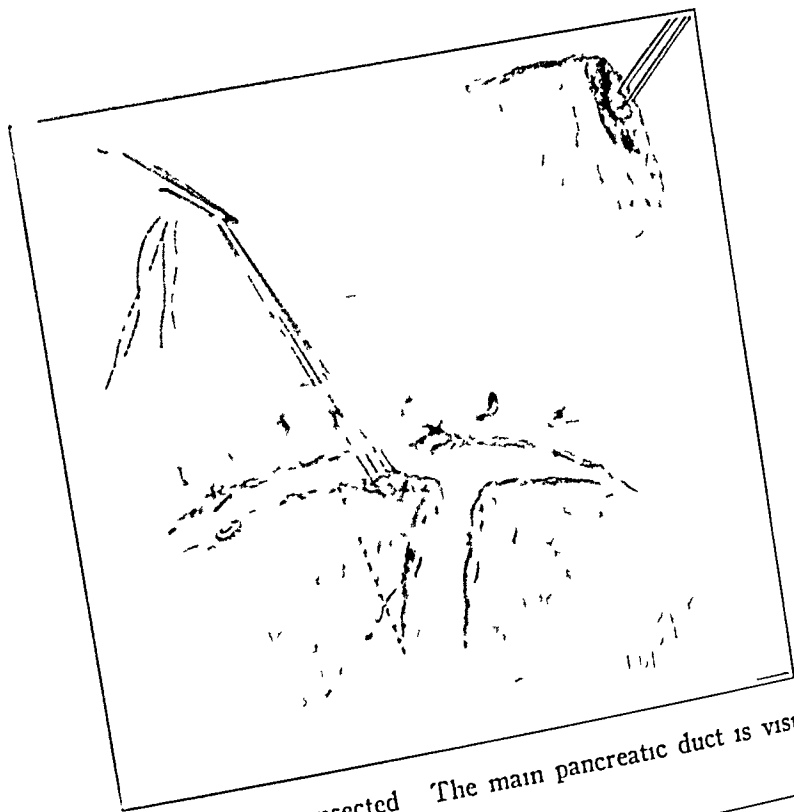


Fig 2—Pancreas transected The main pancreatic duct is visualized

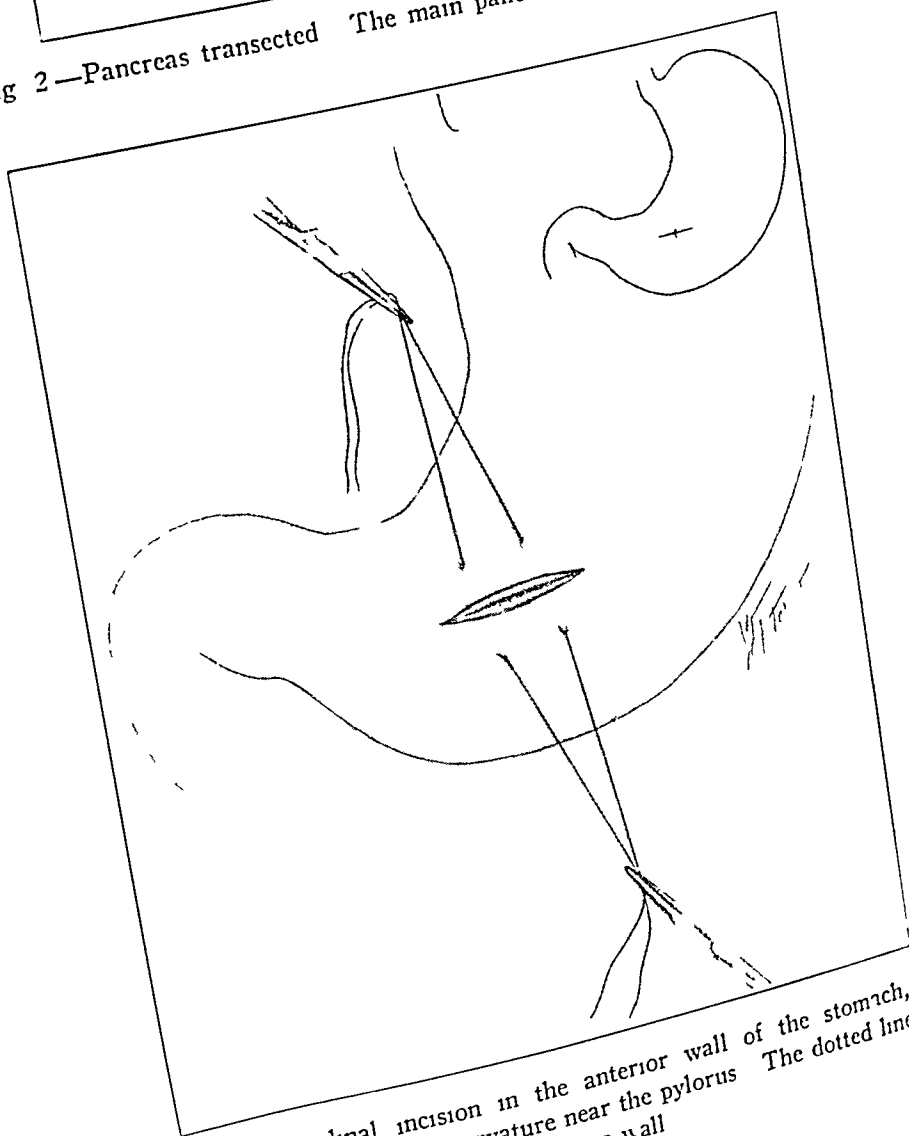


Fig 3—Longitudinal incision in the anterior wall of the stomach, mid way between the greater and lesser curvature near the pylorus The dotted line indicates the incision on the posterior gastric wall

the opening (fig 4) The stay sutures attached to the pancreatic duct were also brought through into the stomach and subjected to tension through the anterior incision in the gastric wall, thus drawing the stump well into the gastric lumen With this traction maintained, the pancreas was anchored into position by tying the sutures which passed through the wall of the stomach (fig 5) This resulted in an everted approximation of the gastric wall to the pancreatic parenchyma Additional sutures were introduced at either end of the incision to fix it permanently in place The abdomen was closed with silk without drainage

Results and Comment—In this series of experiments 32 dogs were used The first 12 dogs were subjected only to pancreaticogastrostomy as described The method proved to be entirely satisfactory and surgically feasible For this reason it was instituted in the remaining dogs as a preliminary step in operations on the ampulla of Vater and the head of the pancreas One dog died of acute hemorrhagic pancreatitis on the third day after the transplant, owing to a technical error Six dogs were killed at appointed times to determine microscopically the condition of the pancreatic parenchyma and to confirm the chemical indications that the pancreatic duct remained patent Proof of the patency of the duct was obtained by injecting fluid into the caudal end of the pancreatic duct and observing its free flow into the stomach

Death subsequent to further surgical procedures occurred in 17 animals The duration of life after operation varied from five to one hundred and seven days Complete postmortem examinations were made routinely In the majority of instances death was due to bronchopneumonia, perforation of a jejunal ulcer or intussusception Eight dogs were still alive from forty-eight to one hundred and sixty-nine days after the two stage procedure

Tables 1 and 2 present data on 6 dogs which survived and 6 which died These animals were subjected to the following two stage procedures first stage, pancreaticogastrostomy, cholecystogastrostomy and ligation of the common duct, and second stage, resection of the head of the pancreas and duodenum and gastroenterostomy

The purpose of the first stage of the procedure was to create a new channel for bile and pancreatic secretions into the gastrointestinal tract In performing the pancreaticogastrostomy, an exploratory incision in the anterior wall of the stomach constituted one step, this anterior aperture was used as a stoma for the cholecystogastrostomy An interval of from ten to twenty-five days elapsed between the first and the second stage of the operation

In every instance marked atrophy and fibrosis of the head of the pancreas were found at the second operation This pathologic alteration was due to the inadequate blood supply to the remaining portion of the pancreas—the result of ligating the pancreaticoduodenal vessels during the transection of the gland at the first operation On the other hand the flow of blood through the implanted portion of the pancreas was sufficient to permit the organ to function normally during the life of the animal This was determined by chemical tests and confirmed by the absence of atrophy and fibrosis at postmortem examination

All the dogs subjected to this experiment were placed on a standard diet³⁴ supplemented by vitamins B C and D They all remained active and well and

34 This was a basal diet given on the basis of 80 calories per dog per kilogram of body weight The approximate ratio was 50 to 60 Gm of carbohydrate 20 to 25 Gm of fat and 18 to 25 Gm of protein This was supplemented by vitamins in the form of yeast (brewer's), cod liver oil and tomato juice administered daily Lecithin choline and extracts of the pancreas were not given

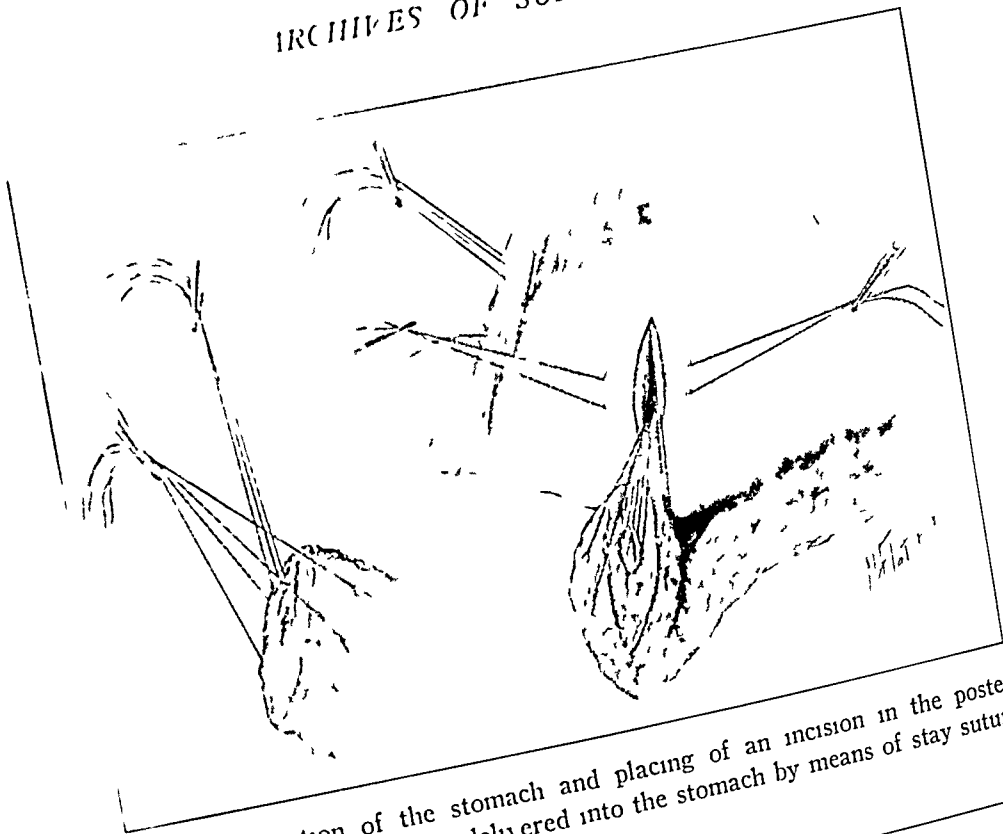


Fig 4—Rotation of the stomach and placing of an incision in the posterior gastric wall The pancreas is delivered into the stomach by means of stay sutures

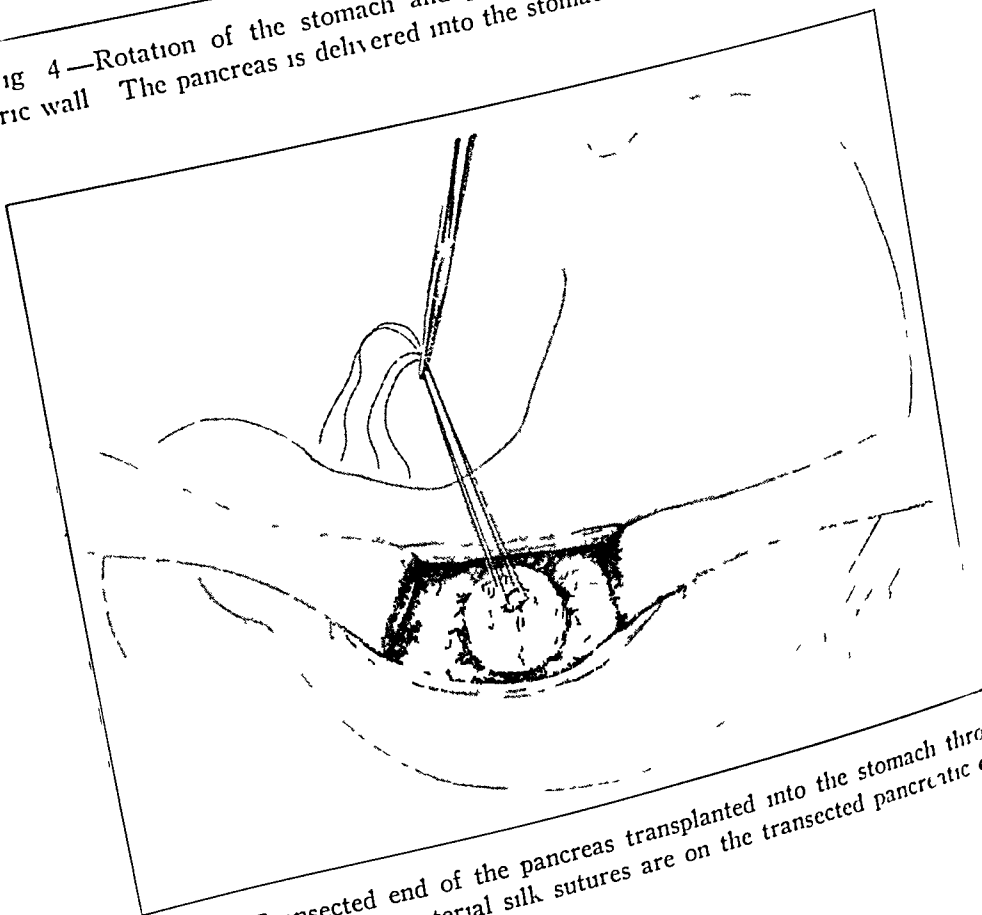


Fig 5—Transected end of the pancreas transplanted into the stomach through the posterior wall The arterial silk sutures are on the transected pancreatic duct

TABLE 1—Data on Six Dogs Which Survived

Dog No	Initial Weight	Present Weight	Days Alive	General Health	Chemical Analysis				Hepatic Analysis			Pancreatic Examination at
					Gastric Intake	Blood Sugar	Urinalysis	I lipid (Quantitative)		Microscopic Examination		
								Per centage	Days After Operation		Hematoxylin and Eosin	
210	22 pounds (10 K _g .)	22 pounds (10 K _g .)	169	Good	Yes	Normal	No sugar	0.2	140	Normal	No	Normal
241	20 pounds (9.2 K _g .)	18 pounds (8.2 K _g .)	126	Good	Yes	Normal	No sugar	3.0	90	Normal	No	Normal
311	20 pounds (9.1 K _g .)	23 pounds (10.4 K _g .)	90	Poor (jejunal ulcer)	Yes	Normal	No sugar	5.1	57	Normal	No	Normal
327	27 pounds (12.3 K _g .)	25 pounds (11.3 K _g .)	88	Good	Yes	Normal	No sugar	4.8	40	Normal	No	Normal
330	28 pounds (12.7 K _g .)	23 pounds (10.4 K _g .)	82	Fair	Yes	Normal	No sugar	7.0	60	Normal	Slight Slight atrophy with fibrosis	Normal
372	21 pounds (9.5 K _g .)	20 pounds (9.1 K _g .)	48	Good	Yes	Normal	No sugar	5.2	30	Normal	No	Normal

TABLE 2—Data on Six Dogs Which Died

Dog No.	Initial Weight	Weight Before or After Death	Days Alive	Chemical Analysis			Hepatic Analysis			Cause of Death	
				Gastric Intake	Blood Sugar	Urinalysis	I lipid (Quantitative)	Microscope Examination			
								Hematoxylin and Eosin	Fatty Infiltration		
203	17 pounds (7.7 kg.)	14 pounds (6.4 kg.)	107	Yes	Normal	No sugar	1.1	Normal	No	Normal	Microscopic pancreatic duct patent
250	20 pounds (9.1 kg.)	18 pounds (8.2 kg.)	90	Yes	Normal	No sugar	1.2	Normal	No	Normal	
254	21 pounds (9.5 kg.)	18 pounds (8.2 kg.)	75	Yes	Normal	No sugar	0.2	Early degeneration	Slight	Normal	Increase connective tissue
27	23 pounds (10.4 kg.)	19 pounds (8.6 kg.)	75	Yes	Normal	No sugar	5.2	Normal	No	Normal	
40	24 pounds (11.0 kg.)	22 pounds (10.0 kg.)	70	Yes	Normal	No sugar	5.0	Normal	No	Normal	Normal
111	20 pounds (9.1 kg.)	10 pounds (4.5 kg.)	60	Yes	Normal	No sugar	5.5	Normal	No	Normal	

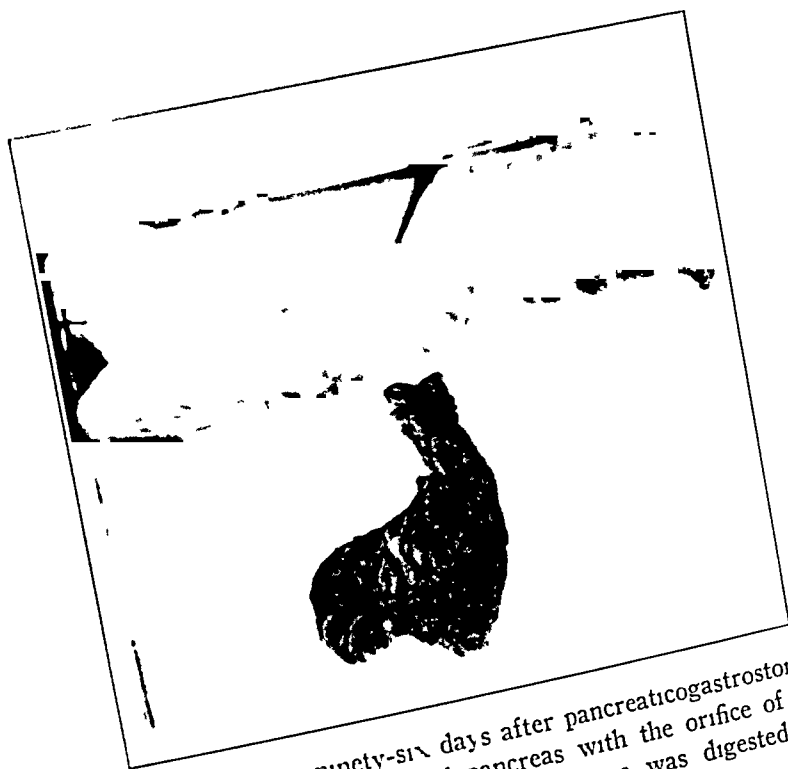


Fig 6—Fixed specimen ninety-six days after pancreaticogastrostomy. Note the normal appearance of the transplanted pancreas with the orifice of the duct cannulized. (The intragastric portion of the pancreas was digested in twenty to twenty-five days.)

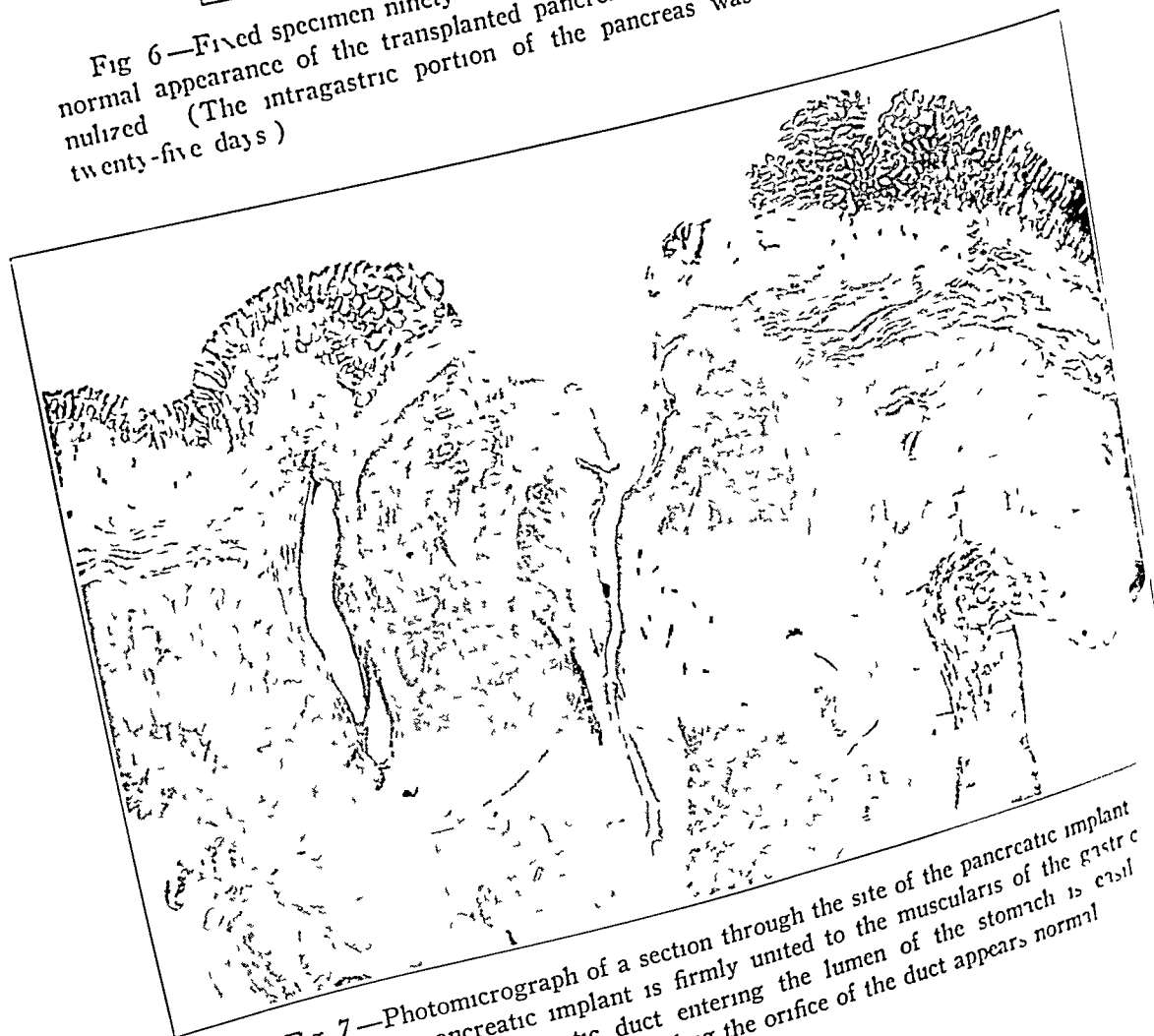


Fig 7—Photomicrograph of a section through the site of the pancreatic implant. Note that the pancreatic implant is firmly united to the muscularis of the gastric wall. The patent pancreatic duct entering the lumen of the stomach is easily demonstrable. The mucosa surrounding the orifice of the duct appears normal.

they remained within 5 pounds (2.3 Kg) of their initial weight except the animals in which a jejunal ulcer developed after the two stage procedure³⁵

After the pancreaticogastrostomy, at intervals of ten to one hundred and forty days, analyses of the gastric contents and of the urine were made, and the value for blood sugar was determined. Since the gastric contents invariably revealed

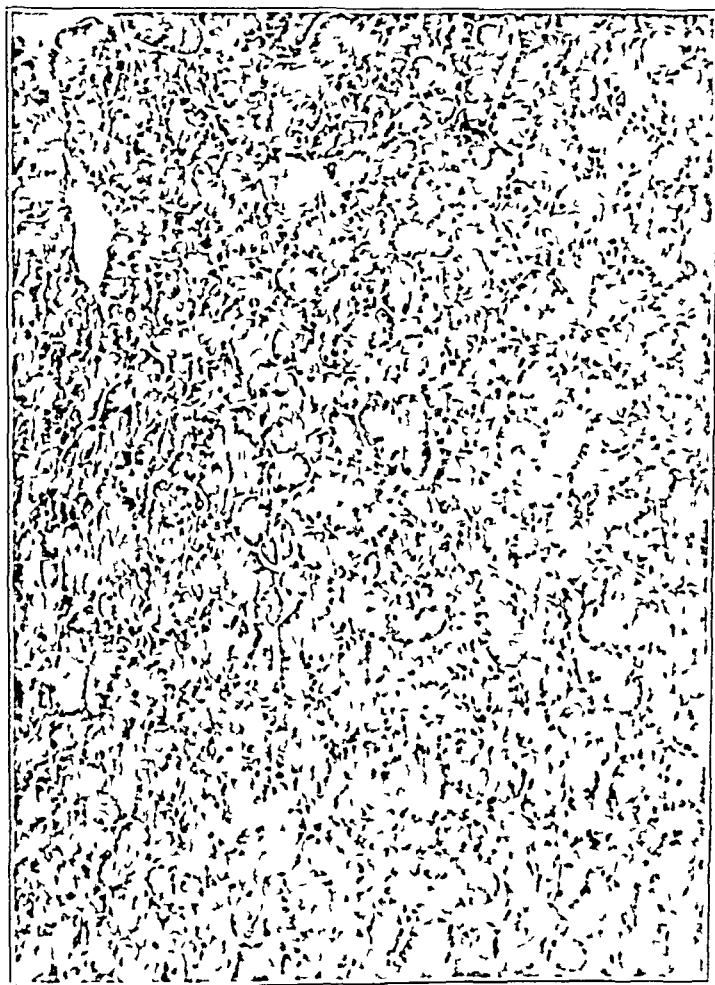


Fig 8—Photomicrograph of the pancreas seventy-five days after pancreaticogastrostomy. The pancreas retains its normal architecture. There is no evidence of atrophy or increase in connective tissue.

the presence of active pancreatic lipase, it must be concluded that the pancreatic secretion reached the stomach. At no time were there more than negligible changes

³⁵ Eiselberg (cited by Markowitz, I. Textbook of Experimental Surgery, New York, William Wood & Company, 1947) found that jejunal ulcer developed in over 25 per cent of animals subjected to pyloric exclusion and gastroenterostomy.

in the value for blood sugar, and repeated analyses of the urine failed to reveal the presence of sugar.

When the abdomen was opened after the first operation or at a specific date to obtain biopsy tissue from the liver, inspection of the site of transplantation revealed a normal-appearing pancreas without perceptible atrophy, firmly united

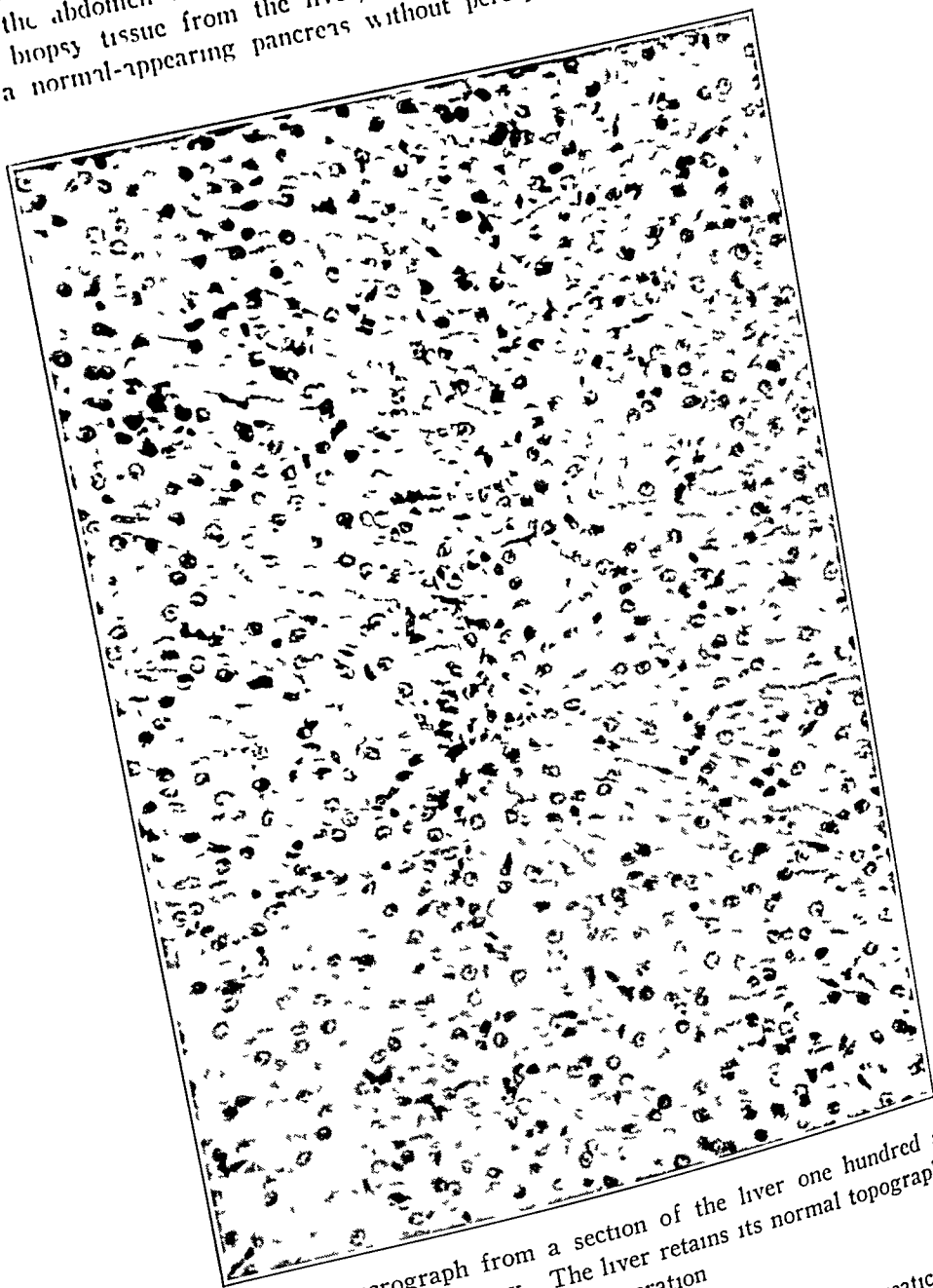


Fig 9—Photomicrograph from a section of the liver one hundred and forty days after pancreaticogastrostomy. The liver retains its normal topography. There is no evidence of fatty infiltration or degeneration.

to the stomach. It was found that the excess intragastric pancreatic tissue projecting into the stomach after implant was digested in twenty to twenty-five days but the orifice of the duct remained patent (fig 6). On microscopic examination serial sections through the site of the pancreatic implant revealed connective tissue union between the pancreas and the musculature

of the gastric wall. The pancreatic acini appeared orderly and without evidence of cellular dissociation or inflammatory cell infiltration. The islets of Langerhans appeared normal. The mucosa around the patent orifice of the pancreatic duct was not ulcerated and appeared normal (figs 7 and 8). It is known that the liver assimilates fat if the intestinal tract is deprived of the external secretion

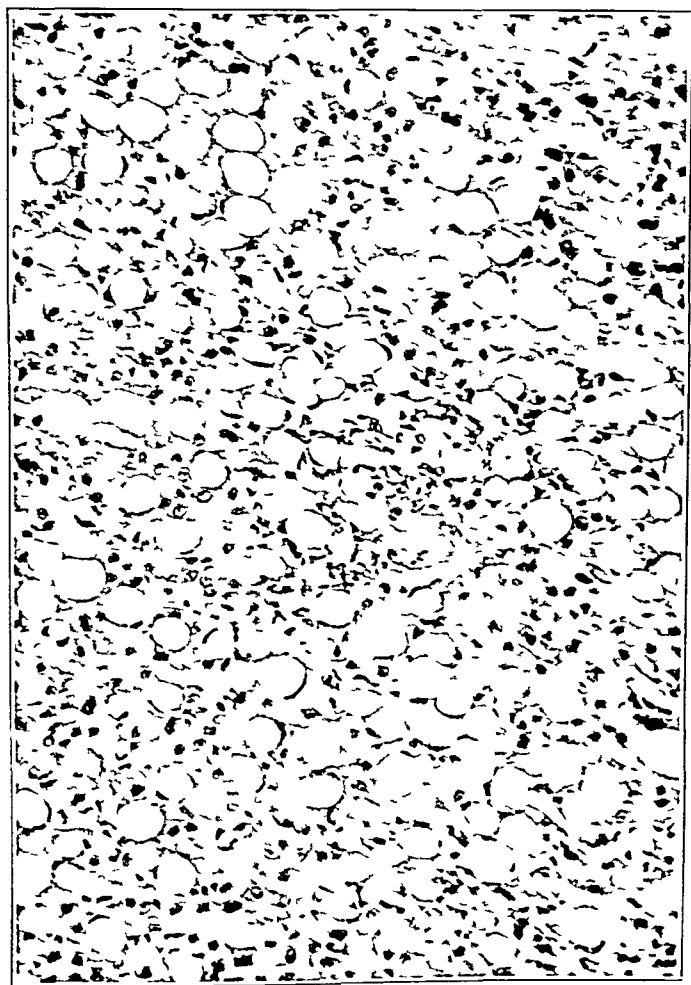


Fig 10—Photomicrograph from a section of the liver sixty days after ligation division of the pancreatic ducts and partial pancreatectomy. The normal hepatic architecture is hardly discernible owing to fatty acid infiltration and degenerative changes in the hepatic cell.

of the pancreas. Therefore, 3 to 10 grams (0.19 to 0.65 Gm.) of tissue for biopsy was taken from the liver at intervals of ten to one hundred and forty days after the first stage procedure and subjected to chemical and microscopic examination.

for lipid deposition to determine whether the implanted pancreatic gland continued to function. With the Bloor³⁶ method and a simplified method introduced by Kaplan and Chaikoff³⁷ the fatty acid content of the liver was found to vary from 3.6 to 6.7 per cent in the "transplant" animals, as compared with the normal value of 3 to 5 per cent.



Fig. 11—Photomicrograph from a section of the liver ninety days after ligation and division of the pancreatic ducts and pancreatectomy. Note the advanced vacuolation and the degenerative changes in the hepatic cell.

Microscopic section of the liver treated with special stains (methyl blue sulfate and sudan III) confirmed these quantitative results, since there was no infiltration of the liver cells with fat. Examination with routine stains (hematoxylin and

³⁶ Bloor, W. R. Oxidative Determination of Phospholipid (Lecithin and Cephalin) in Blood and Tissues, *J. Biol. Chem.* 82:273, 1929.

(Footnote continued on next page.)

eosin) showed that the cords and cells of the liver had retained their normal orderly arrangement. There was little cellular infiltration and no evidence of cellular degeneration (fig. 9).

In order to study the effects of complete exclusion of the external secretion of the pancreas from the intestinal tract, animals were subjected to ligation and



Fig. 12—Photomicrograph of the pancreas sixty days after ligation division of the pancreatic ducts and partial pancreatectomy. There are marked dilatation of the pancreatic ducts and destruction of acini by invading connective tissue.

division of the pancreatic ducts and partial pancreatectomy. The amount of gland resected corresponded as closely as possible to that removed in the trap operation.

37. Kaplan, A., and Chaikoff, I. K.: Liver Lipids in Completely Deprived of Dogs Maintained with Insulin. *J. Biol. Chem.* **105**: 201, 1935.

animals, but the stump was reenforced with omentum and left in situ instead of being transplanted into the stomach. The various secondary procedures which formed a part of the completed operation in the first series of animals were carried out on these 6 dogs also. The animals were subjected to cholecystogastrotomies, duodenal resections and gastroenterostomies in either two or three stages, but they showed less tolerance for these interventions than did the "transplant" animals. Although their diet was the same, these dogs lost weight and exhibited a syndrome consisting of anorexia, exhaustion, intermittent vomiting and foamy stools. Pancreatic lipase was not present in the gastric contents, the values for blood sugar



Fig. 13—Fixed specimen one hundred and seven days after the completed two stage procedure. The photograph shows the site of the pancreatic implant and the stomas of cholecystogastrotomy and gastroenterostomy.

remained within normal limits in spite of the marked pancreatic atrophy, quantitative determinations of the lipid content of the liver showed an increase in fatty acid as high as 8 to 184 per cent. Microscopic studies of the livers of the dogs revealed diffuse fatty infiltration of the hepatic cells, and routine stain demonstrated extensive cellular dissociation. The normal hepatic architecture was hardly discernible. The liver cells were transformed into large vacuoles with small, peripherally placed nuclei. The degenerative changes were diffuse but seemed to be more marked in the periphery of the lobule (figs. 10 and 11).

TABLE 3.—Data on Six Dogs Subjected to Ligation and Devision of the Pancreatic Ducts and Partial Pancreatectomy Without Transplantation of the Pancreatic Stump into the Stomach

Dog No.	Initial Weight (lb.)	Weight before or After Death (lb.)	Days after Operation	Post-operative Course	Gastric Lipase	Chemical Analysis			Hepatic Analysis			Post-mortem Examination of Pancreas		Cause of Death
						Blood Sugar	Urine	Percent Fat at Death	Microscopic Examination	Gross	Microscopic			
												Hematoxylin and Eosin	Infiltration	
90	13 pounds (5.9 kg.)	23 pounds (10.4 kg.)	93	Poor	No	Normal	No sugar	8	Slight atrophy with degeneration	++	Pancreatic cyst with atrophy	Chronic pancreatitis with cyst	Pneumonia	
91	8 pounds (3.6 kg.)	7 pounds (3.2 kg.)	60	Poor	No	Normal	No sugar	12	Atrophy with cellular disorganization	+++	Atrophy	Chronic pancreatitis with atrophy and fibrosis	Cachexia	
92	10 pounds (4.5 kg.)	10 pounds (4.5 kg.)	41	Fair	No	Normal	No sugar	9.6	Moderate degeneration	++	Atrophy with pancreatic cyst	Chronic pancreatitis	Perforated jejunal ulcer	
93	14 pounds (6.3 kg.)	9 pounds (4.1 kg.)	6	Poor	No	Normal	No sugar	11.2	Degeneration and atrophy	++	Atrophy	Chronic pancreatitis	Pneumonia	
111	18 pounds (8.2 kg.)	16 pounds (7.3 kg.)	23	Poor	No	Normal	No sugar	11.3	Slight degeneration	+++	Atrophy	Chronic pancreatitis		
112	11 pounds (5.0 kg.)	6 pounds (2.7 kg.)	10	Poor	No	Normal	No sugar	18.4	Degeneration and atrophy	+++	Irreversible pancreatitis	Diffuse pancreatic necrosis	Pancreatic necrosis	

At autopsy the pancreas was small and exceedingly firm on section, and the ducts were dilated throughout their course. Microscopic examination of the pancreatic parenchyma revealed a marked overgrowth of connective tissue, dividing the disrupted cell groups into lobules. The remaining acini were composed of flat epithelium which appeared vacuolated and atrophic. The islands of Langerhans were numerous and somewhat hypertrophic (fig 12).

For the greater part, chronic pancreatitis with fatty infiltration and early degenerative changes constituted the outstanding pathologic picture. However, in 1 instance hemorrhagic pancreatitis, apparently due to the escape of active enzymes from a retention cyst following ligation of the acini, resulted from the procedure.

In this series of animals life expectancy was materially reduced and death occurred as the result of the added burden of the second stage operations or of an intercurrent infection.

CONCLUSIONS

- 1 By a modification of the Tripodi and Sherwin method the pancreas can be transplanted into the stomach without danger of immediate acute pancreatitis or peritonitis.

- 2 The transplanted pancreas retains its external and internal functions and shows no sign of atrophy.

- 3 Lipid deposition and degeneration of the liver do not follow pancreatic transplantation.

- 4 Complete exclusion of the external secretion of the pancreas by the stated methods produces an abnormal deposition of fat in the liver and concomitant degeneration and atrophy of the liver cells.

- 5 The presented method of conserving the pancreatic secretion offers a favorable means of approach in the radical treatment of malignant lesions involving the periampullary region and the head of the pancreas.

TRAUMATIC SUBCUTANEOUS RUPTURE OF THE NORMAL SPLEEN

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This paper is based on 29 cases of subcutaneous rupture of the normal spleen, due to trauma, observed by us at the Harlem Hospital Connors¹ reviewed the cases in which the condition was treated at the same hospital from 1905 to 1927 inclusive. One of us (L T W) had the opportunity to study many of these cases. The present report covers the period from Jan 1 to Sept 1, 1938. It was thought advisable to review this group of cases and whenever possible to compare them with the cases reported by Connors, since the two series represent a continuous study in one institution over a period of years. Some of the tables to be presented have been included for the sake of completeness, others indicate aspects of the subject that have not been mentioned in the literature. In all cases in the series, operation or autopsy proved the spleen to be the injured organ and histologic section showed normal splenic tissue.

This condition is not as infrequent as one is led to believe by the various reports in the literature. During the period covered by this report there were approximately 20,000 patients admitted to the traumatic service of the Harlem Hospital. Thirty of these patients had rupture of the spleen. This indicates roughly an incidence of 1/666. With the continued increase in the number of automobile accidents this ratio will probably rise.

There is wide variation in general opinion as to the frequency of rupture of the spleen as a complication of intra-abdominal injuries. Mazel² stated that rupture of the spleen occurs in 30 per cent of subcutaneous injuries to the abdominal viscera. Bronaugh³ stated that injury to the spleen occurs in 33.3 per cent of injuries involving abdominal organs. Angle and Kassel⁴ stated the opinion that these figures are high.

From the Surgical Service of the Harlem Hospital.

1 Connors, J. F. Ann Surg 88:388, 1928.

2 Mazel, M. S. Illinois M J 62:170, 1932.

3 Bronaugh, W. West Virginia M J 31:50, 1935.

4 Angle, L. W. and Kassel, H. W. J Kansas M Soc 36:22, 1935.

In studying the incidence of subcutaneous rupture of the spleen, liver, intestines, mesentery and pancreas one finds that splenic injury is more common than is generally believed. Data on the relative frequency of subcutaneous injuries to these structures (table 1) show that the spleen is involved in 47.6 per cent of cases of pathologic conditions of the viscera due to subcutaneous injury.

It is of interest to note that according to our experience seasonal variations are unimportant (table 2). The cases are listed according to the year and month in which the injury occurred.

TABLE 1—Incidence of Rupture of the Spleen

Subcutaneous Rupture	No. of Cases	Percentage
Spleen	30	47.6
Liver	18	28.6
Intestines	11	17.5
Mesentery	3	4.7
Pancreas	1	1.6
Total number of cases	63	100.0

TABLE 2—Seasonal Distribution of Cases of Rupture of Spleen

Year	No. of Cases	Month	No. of Cases
1928	2	January	2
1929	1	February	1
1930	4	March	1
1931	1	April	2
1932	3	May	2
1933	7	June	1
1934	1	July	2
1935	3	August	4
1936	1	September	1
1937	3	October	2
1938 (to September 1)	4	November	2
		December	0
Total number of cases	30	Total number of cases	30

Subcutaneous rupture of the normal spleen may be traumatic or apparently spontaneous. Many authors⁵ have concluded that apparently spontaneous rupture occurs only in the diseased spleen. However, from time to time one finds reports in the literature on spontaneous rupture of the normal spleen. In our 30 cases there was but 1 of supposedly spontaneous rupture. This case was reported by Young⁶ from this hospital. The spleen was normal.

5 (a) Smith, S. *Forensic Medicine*, ed 4, London, J & A Churchill Ltd, 1934. (b) Ledderhose, G. *Die chirurgischen Erkrankungen der Bauchdecken und die chirurgischen Krankheiten der Milz*, in Billroth, C. A. T., 1st ed, p 147. (c) Foucault, P. *J de med de Bordeaux* 102:1138, 1925.

6 Young, R. H. *Ann Surg* 101:1389, 1935.

Trauma then accounts for rupture of the normal spleen in the greatest number of cases. The trauma may vary in type and severity, and the resultant injury to the spleen may not be correlated with the severity of the trauma. The force may be sudden, severe or mild and may or may not be directed against the splenic area. Not infrequently there are associated lesions.

The automobile continues to be the traumatic agent in the greatest number of cases. Table 3 shows how the nature of the trauma varies. Table 4 gives the percentages for this series and that of Connors.¹

TABLE 3—*Trauma in Cases of Splenic Rupture*

Trauma	Present Series (1928-1938)	Connors' Series (1905-1927)
Struck by automobile	15	18
Passengers in automobile accident	5	0
Struck by motorcycle	0	1
Falling		
Out of windows	3	1
To the ground	3	3
Down elevator shaft	0	1
From carriage seat	0	1
Into areaway	0	1
Struck by falling body of another person	0	1
Assault and battery	2	1
Run over by wagon	0	3
Undetermined	1	1
Struck by bicycle	1	0
Colliding with tree	1	0

TABLE 4—*Percentages for Trauma in Cases of Splenic Rupture*

Trauma	Present Series (1928-1938) Percentage	Connors' Series (1905-1927) Percentage
Motor accidents	63.3	39.4
Falls	20.0	21.9
Assault and battery	3.3	3.1
Assault and battery	6.7	3.1
Run over by wagon	0.0	9.4
Undetermined	3.3	3.1
Struck by bicycle	3.3	0.0
Falling body	0.0	3.1
Colliding with tree	3.3	0.0

Correlation of the age incidence with the traumatic agent reveals some interesting and significant facts. There were 9 patients, or 30 per cent between the ages of 5 and 10 years inclusive. Of these, 8 were injured in automobile accidents and the ninth by a fall against the curbstone (table 5).

In the age group from 11 to 20 years inclusive there were 5 patients or 16 per cent. The patients in this group were more capable of handling themselves in respect to automobile injuries. Only 2 were struck by automobiles. The third was injured while riding in an automobile, the fourth was struck by a bicycle and the fifth was injured while coasting.

Alcohol played a prominent role in the injuries of patients aged from 21 to 30 inclusive (7 patients, or 23.3 per cent). Three were hurt by falling while drunk, 1 was involved in an automobile accident while intoxicated, 2 were injured by automobiles, and 1 either fell or jumped from a fourth story window.

Six patients, or 20 per cent, were in the age group between 31 and 40 years, inclusive. Two were victims of assault and battery, 3 were

TABLE 5—Age and Sex of Patient Correlated with Type of Trauma

Age	Sex		Total	Trauma				
	Male	Female		Automobile Accidents	Assault and Battery	Falling	Injury in Coasting	Bicycle Accident
5	2	1	3	3				
6	1		1	1				
8	3	1	4	4				
10	1		1			1		
11	1		1					1
12	1		1	1				
17		1	1				1	
20	2		2	2				
22		1	1	1				
23	1		1			1		
25	1		1			1		
26	1		1			1		
27	1	1	2	1		1		
28	1		1	1				
32	1		1		1			
36		1	1	1				
38	1	1	2	1	1			
39	1		1			1		
40	1		1	1				
43	1		1	1				
47	1		1					
61	1		1	1				
	23	7	30	19	2	6	1	1

TABLE 6—Comparative Age Incidence of the Two Series

Age, Years	This Series (1928-1938) Percentage	Connors' Series (1905-1927) Percentage
0 to 10	30.0	43.8
11 to 20	16.6	25.0
21 to 30	23.3	9.4
31 to 40	20.0	0.4
41 to 50	10.0	12.5

involved in automobile accidents, and 1 fell and injured himself while under the influence of liquor.

In the final age group (43 to 61 years, inclusive) there were 3 patients, or 10 per cent. Two were injured by automobiles, and the cause of injury to the third was undetermined.

A comparison of the age incidence in this series with that in the series reported by Connors reveals a tendency toward a relatively greater incidence in the older age groups. Traumatic subcutaneous rupture of the normal spleen still occurs most frequently in children (table 6).

In table 5 one observes that there were 7 female patients in the 30 cases representing 23.3 per cent of the total number (This is not essentially different from the incidence reported by Connors¹ In his series of 32 cases there were 7 female patients, or 21.8 per cent) Of the 7 females involved 5 were hurt in automobile accidents, the sixth fell from a window and the seventh was injured while coasting

The injury in 19 of the 30 cases was caused by automobile accidents, one finds therefore, that there were proportionately more associated lesions When the traumatic agent was of a sort to cause milder injury, rupture of the spleen alone was not uncommon The position was formerly held that traumatic rupture of the spleen is always accompanied

TABLE 7—Lesions Associated with Rupture of the Spleen

Case No	Associated Conditions								Trauma
	Fractured Ribs	Broken Bones	Lacerated Kidney	Ruptured Lung Hemo pneumo thorax	Injury to Brain	Ruptured Diaphragm	Ruptured Bladder	Ruptured Liver	
1	1	1	1			1			Automobile accident
2	1	1	1	1					Automobile accident
3	1								Automobile accident (passenger)
4	1		1	1	1				Automobile accident
5		1					1		Fall
6	1	1							Automobile accident
7	1	1		1					Automobile accident
8			1		1			1	Fall
9		1							Automobile accident
10								1	Drunk?
11	1	1			1				Automobile accident
12	1		1						Automobile accident
13								1	Automobile accident
14		1							Automobile accident
15	1		1						Automobile accident
16	1								Automobile accident (passenger)
17				1					Automobile accident
	10	8	6	4	3	1	1	3	

by associated lesions The report of Connors and subsequent reports in the literature have shown that this opinion is untenable

There were 17 cases (table 7) in which severe associated lesions were present Of the 17 patients 12, or 70.5 per cent, were struck by automobiles and 2, or 11.8 per cent, were riding in automobiles involved in accidents This makes a total of 14 cases (82.3 per cent) in which the injury was directly or indirectly due to the automobile accident In 2 cases the injury was caused by falls from a considerable height In the last case there was no history of trauma, but we have every reason to believe that the patient was injured while under the influence of liquor

The frequency of the various associated lesions, in the order of their occurrence is given in table 8 There were 10 cases in which the injury was associated with fractured ribs, in 9 of these the lower ribs

of the left side were involved. The frequency of fractured ribs on this side was first noted by Chaher.⁷

Because of the frequency of associated lesions causing diagnostic difficulties in our series of cases, we shall (except in 1 or 2 instances) base our classification of traumatic rupture of the normal spleen on the cases in which no complication was present.

There is considerable variation in the clinical manifestations of splenic rupture, due to the character of the internal concealed hemorrhages which dominate the symptoms, classification, therefore, is not easy. It is clear that any classification must be somewhat elastic.

Mazel² divided the cases into the following groups:
1 Cases of immediate hemorrhage. The hemorrhage may be so copious as to cause sudden collapse and death before any steps can be taken.

2 Cases of less severe hemorrhage. A moderate hemorrhage develops, and all the signs of internal hemorrhage are present.

TABLE 8—Complications in Order of Frequency

Associated Lesions	No. of Cases
Fractured ribs	10
Broken bones (simple or compound fractures)	8
Lacerated kidney	6
Hemothorax, pneumothorax, lacerated lung	4
Cerebral complications, fractured skull, lacerated brain	3
Ruptured liver	3
Ruptured urinary bladder	1
Ruptured diaphragm	1

3 Cases of delayed hemorrhage. The signs of internal hemorrhage are not obvious for days or weeks.

In our opinion there are five distinct clinical types, dependent on the rate of hemorrhage:

1 Massive hemorrhage, causing almost immediate or sudden death.

2 Acute hemorrhage, producing shortly after the injury a state of shock which rapidly becomes deeper.

3 Repeated small hemorrhages. The patients enter the hospital in good condition but show signs of slow progressive hemorrhage—increasing anemia, a rising pulse rate, a fall in blood pressure and progressive weakness.

4 Late hemorrhage. The patients have an initial injury from which they recover. After a period of relief from symptoms they may suddenly go into shock, showing signs of acute internal concealed hemorrhage—or they may have a recurrence of signs and symptoms of repeated small hemorrhages. They may gradually become worse, showing signs of increased hemorrhage over a period of days or weeks.

⁷ Chaher, A. Lyon chir. 24 69, 1927

5 Spontaneous cure The patients show no signs of hemorrhage and suffer only localized pain, which soon disappears

In this series there were no cases of massive hemorrhage, although such cases have been reported in the literature⁸ The pathologic condition consists of severe lacerations of the spleen Parts of the organ may be found lying free in the abdominal cavity The vessels in the hilus or the pedicle are usually torn Tears involving the hilus or the pedicle do not necessarily cause death, as is illustrated by Armitage's⁹ case A badly fragmented spleen sometimes may cause only symptoms of acute or delayed hemorrhage

In the group in which acute hemorrhage occurs, the patients, although brought to the hospital shortly after the accident, are in shock on admission The condition of the patient becomes worse as the shock becomes deeper This is illustrated by the following case

CASE 18—On July 12 1930, a boy aged 5 years was brought to the hospital complaining of pain in the back and abdomen One hour before admission the patient was said to have been struck by an automobile At no time, however, was he unconscious Physical examination revealed him to be in shock The pulse rate was 116 The temperature was 101 F There was a tender mass in the left upper abdominal quadrant The urine was normal A diagnosis of rupture of the spleen was made and splenectomy was done The boy made an uneventful recovery The condition in this case was typical of the group The spleen was severely lacerated, and in some regions the tear involved the hilus

Renton¹⁰ described a similar case Mulloy¹¹ also reported a similar case in which a fragment of spleen was found lying free over the bladder The patients in both cases were adults

In cases of "repeated small hemorrhage," after the initial injury the patient's condition gradually becomes worse, with obscure abdominal symptoms and progressive weakness until shock intervenes or until the internal concealed hemorrhage becomes evident and surgical intervention is begun Ten of our 14 cases in which no complication was present belong in this group Eight of the patients were males and 2 were females Their ages varied from 8 to 50 years Case 19 is typical of this group The pathologic condition is variable The spleen may or may not be enlarged by a subcapsular hemorrhage The capsule may show one or more rents scattered over the surface of the spleen These lacerations involve the splenic parenchyma, vary from 2.5 to 7.5 cm in length and may contain blood clot The splenic capsule may not rupture, but there may be a subcapsular hematoma, which increases in size

8 (a) Berger E Arch f Clin Chir 68 768 1902 (b) Bailey H Brit J Surg 17 417, 1930

9 Armitage, G Brit J Surg 17 335 1929

10 Renton, M W Brit M J 2 470 1934

11 Mulloy J P Canad M A J 34 680 1936

CASE 10—A 39 year old man was admitted to the hospital on July 8, 1933 because of vomiting and abdominal pain of one day's duration. On the day before admission, while sitting on a park bench, the patient vomited food. The vomitus contained no gross blood. Immediately afterward he experienced severe sharp sticking periumbilical pain. The pain persisted but began to radiate to the left side of the back and to the left shoulder. On coughing the pain radiated also to the right shoulder. Since the onset of the attack, he had become progressively weaker and short of breath. He had several watery stools containing fresh blood. On the night before admission he had three chills. He had been "on a drinking spree" for three months prior to admission.

There had been a stab wound of the abdomen twenty-five years previously and lobar pneumonia one year prior to admission. During the past year he had been treated for "stomach trouble" with powders and he was placed on a diet for convalescent patients with gastric ulcers. No roentgenograms were taken at this time.

Physical examination revealed him to be well nourished and well developed. He was dyspneic, cyanotic and acutely ill. There was dullness at the base of the right lung. The pulse rate was 110, the respiratory rate 30, the temperature 100 F and the blood pressure 120 systolic and 82 diastolic. The abdomen was distended and tender throughout. The value for hemoglobin was 70 per cent. The erythrocyte count was 4,400,000 and the leukocyte count 13,850 per cubic millimeter.

After a clysis the patient began to show signs of improvement. A roentgenogram of the abdomen showed no free air under the diaphragm. An abdominal tap gave negative results. A diagnosis of acute abdominal disease was made. It was decided to observe the patient for a short period. The next morning, twenty hours after admission, the pulse rate rose to 120 and the temperature to 102.8 F. The abdominal distention increased. The patient finally went into shock. Operation and transfusion were then done. At operation a ruptured spleen was found. The patient died one-half hour after the operation.

There is a group of cases in which late hemorrhage takes place and in which there is a period of symptomatic relief, termed by Baudet¹² "the latent period." The asymptomatic period is terminated by some minor incident, such as straining at stool or muscular spasm, or even for no apparent reason. Contrary to general opinion, the second hemorrhage may not begin dramatically with acute symptoms of loss of blood but may have an insidious onset.

There were 2 cases of late hemorrhage. Both patients were women, aged 22 and 36 respectively. McIndoe¹³ has collected 46 similar cases, in which the ages of the patients varied from 8 to 63 years. Only 4 of the patients were females. Other cases have been reported in the literature.¹⁴

12 Baudet, R. *Méd prat* 3 565, 1907
13 McIndoe, A. H. *Brit J Surg* 20 249, 1932, *Proc Staff Meet*, Mayo Clin 3 365, 1928

14 Wenger, L. *Brit M J* 1 1235, 1936 Gardner, R. *ibid* 1 416, 1937
Wilson, F. *Lancet* 1 1236, 1927 Ryan, C. E. *Wisconsin M J* 32 523 1933
Cellan-Jones, C. J. *Brit M J* 2 700 1928 Livingston, I. *ibid* 2 16, 1930
Dawson-Walker, E. F. *Lancet* 1 523, 1931 McIndoe¹³

CASE 20—A 36 year old woman was admitted to the hospital on March 12, 1937, complaining of pain in the left side of the chest and the left shoulder. Two weeks previously she had been in an automobile accident and had been unconscious for a short time, but had recovered in a few days. At that time she had had some tenderness in the left upper quadrant of the abdomen, which had disappeared. On the day of admission while sitting in a theater, she suddenly had a sharp pain in the left side of the chest and fainted. She regained consciousness but noticed that she was short of breath and that the pain was radiating to the left shoulder. She was nauseated but did not vomit. Her past history was irrelevant except for an oophorectomy five years before admission. Physical examination revealed her to be acutely ill. The temperature and the pulse rate were normal. The blood pressure was 90 systolic and 74 diastolic. There were tenderness and rigidity in the left upper abdominal quadrant. The urine was normal. The value for hemoglobin was 65 per cent. The erythrocyte count was 2,900,000 and the leukocyte count 6,100 per cubic millimeter. The abdomen was tapped, and blood was revealed in the left upper quadrant. This confirmed the diagnosis of intra-abdominal hemorrhage.

A diagnosis of acute pancreatitis was accordingly made. At operation a ruptured spleen was found. After a splenectomy and transfusion the patient made an uneventful recovery.

CASE 16—This case is interesting because of the fact that the asymptomatic period was broken by a recurrence of symptoms. On June 25, 1938, a woman aged 22 was admitted to the hospital complaining of pain in the left side of the chest, radiating to the left shoulder of one day's duration. Three weeks previously the patient had been involved in an automobile accident, sustaining a fracture of the eighth rib on the left. However she was completely asymptomatic three days after the accident. One week before admission she began to have pain in the left side of the chest and general malaise. Three days later she again became asymptomatic and remained so until the onset of the present illness. Physical examination revealed that she was not acutely ill. The temperature, pulse rate and respiratory rate were normal. There was dulness at the base of the left lung, with bronchial breathing over it. The abdomen showed tenderness and spasm in the left upper quadrant. A roentgenogram of the chest revealed a high diaphragm on the left side and a fracture of the left eighth rib. The urine was normal. The value for hemoglobin was 45 per cent. The erythrocyte count was 2,700,000 and the leukocyte count 21,300 per cubic millimeter. Because of the findings in the chest a diagnosis of pneumonia was made. A thoracic tap revealed bloody fluid. The abdominal symptoms became more pronounced. A diagnosis of rupture of the spleen was made. Laparotomy confirmed this diagnosis. The patient recovered after a splenectomy.

The pathologic changes in cases of this type consist of (1) minor superficial capsular rupture with ecchymosis and slow hemorrhage, (2) intrasplenic hematoma and subcapsular hemorrhage with subsequent capsular rupture and (3) capsular and parenchymal rupture with an encapsulated perisplenic hematoma. Frequently the surrounding organs especially the omentum, tend to wall off the lesion.

Of the final group of cases, in which "spontaneous cure" occurs, we know of no instances in this hospital. In 3,000 autopsies our pathologist has seen no evidence of traumatic cysts of the spleen although such

cysts have been reported.¹⁵ Instances of spontaneous cure have been noted. A case reported by Hunter¹⁶ in which operation was performed proves that this may take place. Gordon-Watson¹⁷ described 2 spleens, 1 of which belonged to a woman aged 30 who fell 9 14 meters and fractured her femur. Autopsy, performed ten days after the accident, revealed that the spleen was torn across but that there was a firm scar between the lacerated surfaces. The other specimen was removed post mortem from a woman aged 30 who had been run over by an automobile and had died sixty hours after the accident. A rent in the spleen was closed by a firm clot. Had these 2 patients lived, then cases might have fallen into the group in which late hemorrhage is the distinguishing feature.

The diagnosis of subcutaneous rupture of the normal spleen is not easy. There are no signs or symptoms pathognomonic of this condition, one must, therefore, consider each case on its own merit. The symptoms and signs of rupture of the spleen are chiefly those of local injury and those of hemorrhage, shock and peritoneal and diaphragmatic irritation.

Abdominal pain is the most common complaint. This pain is usually sharp and lancinating and is localized in the left upper quadrant. However, it may be described as generalized abdominal soreness and sometimes more acute in the other quadrants. All the patients either entered with this symptom or had it while under observation.

The radiation of this pain to the left shoulder (Kehr's sign¹⁸) is not uncommon. It occurred in 3 cases. In 1 case the pain radiated to the right shoulder when the patient coughed. Pain in the left shoulder also occurs in association with other conditions in which there is irritation of the diaphragm. The presence of Kehr's sign is not dependent on the quantity of blood in the abdominal cavity. In the case in our series in which the most blood was observed in the abdominal cavity this sign did not appear.

Pain in the chest occurred in 2 cases but was associated with fractured ribs on the left side in 9. In the other 3 it was localized to the left side and was not increased by respiration or coughing.

The symptom next in order of frequency is dyspnea. Eight of our patients complained of being "short winded" or had some form of respiratory distress. This distress may be due to diaphragmatic irritation, injury to the chest wall or acute loss of blood.

¹⁵ Novak, E. *Surg, Gynec & Obst* 45 586, 1927. Starr, F. N. G. *Ann Surg* 98 919, 1933.

¹⁶ Hunter, E. A. *Brit M J* 2 256, 1935.

¹⁷ Gordon-Watson, in Choyce, C. C. *A System of Surgery*, ed 2. London: Cassell & Co., 1923, vol 2, p 114.

¹⁸ Kehr, cited by DaCosta, J. C. *Modern Surgery, General and Operative*, ed 10, Philadelphia, W. B. Saunders Company, 1931, p 984.

Vomiting occurred in 3 cases and diarrhea in 2. The patients in whose cases we observed vomiting and diarrhea had been drinking alcoholic liquors prior to admission, so that these symptoms may have been related not to the splenic injury but to gastroenteritis.

The physical findings are more helpful. In all cases there were abdominal tenderness and spasm. The point of maximum tenderness was not necessarily localized to the splenic area. The results of abdominal examination were further obscured by the fact that the trauma which produces the splenic injury may cause contusion of the abdominal wall. More important is the fact that in no case were there any external marks on either the abdomen or the back.

Table 9 gives the location of the region of tenderness and spasm in our cases.

During the past few years we have been looking for an instance of a positive Cullen sign.¹⁹ As yet none has been noted.

Shifting dullness and Ballance's²⁰ sign were noted in only 6 cases. Abdominal distention, usually soft, occurred in 6 cases.

TABLE 9—*Localization of Abdominal Tenderness and Spasm*

Region	Number of Cases
Left upper quadrant	14
Generalized	6
Both upper quadrants	5
Periumbilical	1
Both lower quadrants	2
Right side	2

An abdominal mass in the left upper quadrant was noted in 1 case.

In another case a flat roentgenogram of the abdomen showed a dense shadow under the left leaf of the diaphragm.

Three patients fainted prior to admission. They quickly regained consciousness. Seven patients were brought to the hospital unconscious and in deep shock. All of these had severe associated lesions. All patients regained consciousness while under observation.

The temperature on admission varied from subnormal to 103 F. In general, patients who had severe associated lesions and who were admitted unconscious or in shock tended to have either a subnormal or a normal temperature.

The circulatory system showed wide variations. Patients admitted in shock showed a rapid, thready pulse, low blood pressure and low pulse pressure. Of the 17 patients with associated lesions only 3 showed a normal blood pressure and pulse rate. Of the patients with-

19 Cullen, T. S., in *Contributions to Medical and Biological Research*, Dedicated to Sir William Osler, New York, Paul B. Hoeber, Inc., 1919, p. 420.

20 Pitts, B., and Ballance, C. A. *Tr. Clin. Soc. London* 29:77, 1896. *Lancet* 1:485, 1896.

out associated lesions only 1 entered with a low blood pressure and pulse rate. In general the pulse rate varied between 100 and 140 and the blood pressure from normal to 64 systolic and 40 diastolic. The diagnosis of internal hemorrhage in the case of a patient admitted to the hospital in shock is extremely difficult, and a careful observation of the change in blood pressure and the increase in pulse rate will soon impress the observer, so that adequate measures may be taken.

Examination of the cellular elements and the hemoglobin content of the blood is important. The erythrocyte count and the value for hemoglobin may be normal, but in all except 1 case in our series the latter was low, ranging from 40 to 80 per cent. In the case in which the value for hemoglobin and the red blood cell count were normal the patient was in shock. In all the other cases the red blood cell count ranged from 2,400,000 to 4,400,000 per cubic millimeter. More important is the change noted in the number of red blood cells after repeated determinations. The white cell count ranged from 6,000 to 23,850 per cubic millimeter and not infrequently failed to rise with increasing temperatures.

The urine was normal in all but 7 cases. In these 7 cases it contained blood, and splenic rupture in these cases was associated with laceration of the kidney or bladder. However, one should not be content with a diagnosis of ruptured kidney merely because the urine is pathologic, but should look for evidence of concealed hemorrhage.

There are certain diagnostic procedures which facilitate the diagnosis of rupture of the spleen. Burke and Madigan²¹ reported a case of ruptured spleen in which the patient was given colloidal thorium dioxide. They concluded that thorium dioxide is of practical use in the diagnosis of traumatism of the liver and spleen when physical signs are observed. They claimed that this substance has no deleterious effects even when given intravenously. Damage to the liver and spleen does not contraindicate its use. A dose smaller by half than the usual dose will give satisfactory results in four hours. We do not endorse this procedure, because it is both slow and dangerous.

In our hands the abdominal tap has proved to be of invaluable aid in the diagnosis of subcutaneous injury of the abdominal viscera. In fact, we feel that it is inexcusable to neglect to make an abdominal tap in all cases in which intra-abdominal complications are suspected. This is especially true in cases in which severe associated lesions mask the abdominal complications. In 15 cases of rupture of the spleen the abdominal tap was employed, it gave positive results in 13. It was employed in 1 case of subcapsular rupture of the spleen, and in this case it gave negative results.

²¹ Burke, W., and Madigan, J. *Radiology* 21: 580, 1933.

We have ample evidence to show that the finding of blood by abdominal tap is indicative of intra-abdominal injury. In 3 cases of contusion of the abdominal wall the abdomen was tapped and no blood was obtained. In 1 of these cases there were subsequently normal findings. In the second case postmortem examination showed no intra-abdominal injury.

We have had 3 cases of "false positive" results, in 2 of which there were ruptured kidneys. In both these cases exploration revealed a large retroperitoneal hematoma. In the third case there were signs of concealed hemorrhage. In this case (case 21) autopsy showed bleeding into the mediastinum.

In the cases of 2 patients with rupture of the spleen, the results of the abdominal tap were negative. One case (case 19) has been reported. The other is given in detail below.

CASE 8—A 25 year old man was admitted to the hospital on Oct 29, 1933, after an accident in which he fell from a window. He was conscious but not rational. Physical examination revealed him to be well developed and well nourished. The pulse rate was 70, the respiratory rate 20 and the blood pressure 116 systolic and 90 diastolic. There was no bleeding from the nose and mouth. The remainder of the examination gave normal results. The urine showed albumin and red blood cells. The value for hemoglobin was 75 per cent. The erythrocyte count was 4,000,000 and the leukocyte count 7,900 per cubic millimeter. On admission, a spinal tap revealed a bloody fluid. On the day after admission tenderness in both costovertebral angles was found. A roentgenogram of the chest suggested pneumothorax on the right side. The pulse, which up to this time had been normal, began to rise, reaching 120, and the blood pressure fell to 94 systolic and 60 diastolic. An abdominal tap was reported to give negative results. Because of the hematuria and the bilateral tenderness in both costovertebral angles a diagnosis of laceration of the kidneys was made. On the fourth day after admission the patient began to have abdominal pain and dyspnea and died suddenly. Postmortem examination revealed ruptures of the liver, kidneys, spleen and diaphragm. There were a subarachnoid hemorrhage and hemothorax. The abdominal cavity contained about 500 cc of blood.

From our experience in these cases we have learned that if an abdominal tap gives negative results and the patient continues to show signs of concealed hemorrhage the tap should be repeated.

Our experience with the abdominal tap has been satisfactory, and we do not hesitate to use it. It is especially helpful in cases in which the diagnosis is obscure, in cases in which the patient is admitted unconscious and in shock and in cases in which the physical findings are obscured either by fractured ribs or by concealed hemorrhage into cavities of the body other than the peritoneal.

The diagnosis of subcutaneous rupture of the spleen is not an easy one to make. When the history of trauma bears a direct relation to the chain of symptoms of acute abdominal pain and weakness and to the finding of abdominal tenderness and spasm with a rapid pulse and low blood pressure, a presumptive diagnosis of rupture of the spleen

may be made. The laboratory findings may or may not show evidence of acute loss of blood. Although Kehr's, Ballance's and Cullen's signs are helpful when present, their absence is of no significance.

There are many conditions which may obscure the diagnosis of rupture of the spleen. Contusion of the abdominal wall gives a picture similar to that of subcutaneous splenic rupture, however, in cases of contusion the pulse rate, blood pressure and blood cells are generally normal.

Fracture of the lower ribs on the left side with shock gives a clinical picture identical with that associated with rupture of the spleen. Not infrequently fracture of these ribs is associated with rupture of the spleen. In such a case the finding of blood in the peritoneal cavity and tapping the abdomen are of great importance.

The abdominal tap also aids in localization of the concealed hemorrhage. A patient with abdominal signs and symptoms and evidence of acute loss of blood may be bleeding into cavities other than the peritoneal.

The following case proved not to be an instance of rupture of the spleen, although this diagnosis was made preoperatively. An exploratory laparotomy was performed because blood was obtained on abdominal tap. The case shows how careful one must be not to make a mistake.

ILLUSTRATIVE CASE—A 60 year old man was admitted to the hospital on Sept 22, 1938. He was said to have fallen down a flight of stairs. On admission he appeared acutely ill and was confused and drowsy. The temperature was 99.2 F. The pulse rate was 100, and the quality of the pulse was fair. The blood pressure was 96 systolic and 78 diastolic. There was a small laceration of the scalp over the epigastrium. The value for hemoglobin was 60 per cent. The erythrocyte count was 3,500,000 and the leukocyte count 8,600 per cubic millimeter. The urine was normal. An abdominal tap revealed blood. A tentative diagnosis of rupture of the spleen or of the liver was made, but after the patient had been in the hospital for two hours he began to improve mentally. However, subcutaneous emphysema developed over the left side of the thoracic wall. The pneumothorax reading was -2. At this time it was found that there was a fracture of the eighth, ninth and tenth ribs on the left in the midaxillary line. Underwater drainage was instituted for tension pneumothorax. Because of the positive result of an abdominal tap, an exploratory laparotomy was done with the region under local anesthesia, but no intra-abdominal lesion was found. The patient died nine hours after the operation. Postmortem examination revealed multiple fractures of the ribs, laceration of the lung and multiple contusions of the thoracic wall and of the lung.

An exact diagnosis cannot be made except on the basis of probability. As we have shown that the spleen is involved in 50 per cent of cases of intra-abdominal complications, the most likely diagnosis is that of rupture of the spleen. However, we have been misled, as the following case will show.

ILLUSTRATIVE CASE — A 12 year old boy was brought to the hospital on Sept 9 1938 complaining of generalized abdominal pain Shortly before admission he had been struck by an automobile He was unconscious On admission he was cooperative and complained of pain and shortness of breath The past history, except for the usual diseases of childhood, was irrelevant Physical examination revealed the boy to be well developed and well nourished The temperature was 99 F the pulse rate 110, the respiratory rate 30 and the blood pressure 130 systolic and 80 diastolic Tenderness and rigidity were present in both upper quadrants of the abdomen The urine was normal The value for hemoglobin was 70 per cent The red blood cell count was 3,800,000 per cubic millimeter While under observation the patient seemed to become more anemic and the pulse rate began to rise Abdominal tap showed blood in the left upper quadrant Operation revealed a laceration on the posterior surface of the right lobe of the liver This rent was packed The patient was given a slow drip transfusion He made an uneventful recovery and was discharged on October 2

Rupture of the spleen is an acute abdominal emergency, and as such has to be differentiated not only from other intra-abdominal lesions but from lesions involving concealed hemorrhage into other cavities of the body A study of the cases in which we have missed the diagnosis will bring out the complexity of this problem

The diagnosis was missed in 7 of our 30 cases It seems desirable, therefore to include table 10, in which are listed the cases in which a mistaken diagnosis was made Perforated peptic ulcer was the most common erroneous diagnosis, probably owing to the fact that no history of trauma was obtained In 2 cases the history of trauma was not readily linked with the subsequent chain of events, in 1 case, therefore, a diagnosis of acute hemorrhagic pancreatitis was made, and in another, because of the thoracic findings, the diagnosis was that of pneumonia The diagnosis is most frequently missed when the history of trauma is not obtained or, if obtained, is disregarded because the possibility of late hemorrhage is not kept in mind Other cases have been reported in which the preoperative diagnosis was acute appendicitis,²² ruptured ectopic pregnancy (Rugnave²³) or cholecystitis²⁴ Splenic rupture may also simulate rupture of the left kidney, of the liver or of a gastric ulcer²⁵

Finally, associated lesions may obscure the signs and symptoms of intra-abdominal hemorrhage In 1 case we were satisfied with a diagnosis of laceration of the kidney because no blood was obtained on abdominal tap In another case the abdominal findings were masked by fractured ribs on the left side The positive results of an abdominal

22 Thomas, G B Brit M J 2 1100 1935

23 Rugnave, cited by Stretton J L Brit M J 1 901 1926 Wohlgenuth, K. Berl klin Wchnschr 2 734 1921

24 Wallace, H K J Missouri M A 21 18 1924

25 Heineck, A P Illinois M J 56 205 1929

tap were disregarded, as in case 1. Bleeding not only from other types of intra-abdominal lesions but into other cavities of the body may complicate the diagnosis.

In conclusion, we may say that the diagnosis of subcutaneous rupture of the normal spleen is difficult because there is considerable variation in the clinical manifestation of this condition, owing to the character of the internal concealed hemorrhage which dominates the symptoms. The diagnosis is missed most frequently when no history of trauma is obtained or, if obtained, is disregarded because the possibility of late hemorrhage is not kept in mind. Other conditions, such as laceration of the left kidney, fractured ribs or traumatic pleurisy, may mask the presence of a ruptured spleen. The abdominal tap is of invaluable aid in the diagnosis of this condition, and when the results are negative it should be repeated if conditions warrant it.

TABLE 10—*Diagnosis of Splenic Rupture*

Case Number	History of Trauma	Diagnosis on Admission	Preoperative Diagnosis	Result
16	Yes	Pneumonia	Ruptured spleen	Recovered
19	No	Perforated peptic ulcer	Same	Died
10	No	Perforated peptic ulcer	Same	Recovered
23	No	Ruptured kidney	Same	Recovered
8	Yes	Compound fracture of left tibia, fibula and humerus, fracture of left lower ribs	Same	Died
1	Yes	Acute hemorrhagic pancreatitis	Same	Recovered
20	Yes			

The treatment of traumatic rupture of the spleen is surgical. Berger^{sa} has shown that conservative treatment is fatal in 93 per cent of cases. Operative intervention, therefore, is imperative, and any delay may tend to increase the operative risk.

The preoperative treatment of this condition is directed to the establishment of an accurate diagnosis and the preparation of the patient for operation. The treatment, to be sure, must be different in individual cases. However, no patient suspected of having a ruptured spleen is given a preoperative enema. The clot formed in a bleeding tend to cause a more vigorous hemorrhage.

If shock is present, it is treated in the usual manner. From our experience with other acute abdominal conditions, we have learned that if a slow drip blood transfusion is started as soon as the diagnosis is established the patient will be in a better condition to undergo the surgical procedure. This treatment is more justified because in all cases either transfusion or autotransfusion was done at operation or postoperatively. The "blood bank" has been of considerable aid in these emergencies.

There are two schools of thought concerning the time at which operation should be performed. Connois¹ stated "Immediate operation should be performed regardless of patient's condition and splenectomy is the operation of choice." With this opinion we agree. Armitage² and McIndoe,³ on the other hand, have stated the opinion that steps should be taken to combat shock for "to operate on a patient suffering with systematic shock is unpardonable." One must remember that to delay an operation in order to pour blood into a person who is having a severe intra-abdominal hemorrhage may gain little and may delay operation to such a point that no operative procedure can be carried out. We feel that splenectomy should be done as soon as the diagnosis is made although supportive measures, such as a slow drip transfusion and intravenous administration of fluid, are invaluable and should be begun simultaneously.

The operation of choice is splenectomy, although splenorrhaphy or tamponade or a combination of both has been done. The latter procedures, however, should be discarded in favor of splenectomy.

Tamponade is uncertain, and the bleeding may not be adequately controlled. The abdominal wound in such cases is usually weak. Berger's²⁶ statistics include data on 10 cases in which this procedure was used, with 1 death. Quenu²⁷ reported 15 cases, with 2 deaths.

Splenorrhaphy, first done by Lamarchia²⁸ in 1896, is not advisable because the spleen is composed of friable tissue and is located in a region not readily accessible. The suture line may be reinforced with omentum as advocated by Gourrin²⁹. This procedure has been reported to have a mortality ranging from 25 to 50 per cent. Lotsch³⁰ reported a 37.7 per cent mortality.

Splenectomy, the operation of choice, was first done by Roddick. The first successful splenectomy for traumatic splenic rupture was done by Rieweues³¹ in 1892. The pancreas should be avoided, for injury to this organ may result in formation of a pancreatic fistula or may cause digestion of the edges of the wound with eventual evisceration. We advise splenectomy in cases in which there is subcapsular hemorrhage without rupture of the capsule. Although such lesions may resolve, the danger of subsequent rupture is great. The following case represents our experience with this condition.

26 Berger, E. Arch f Klin Chir 68 863, 1902

27 Quenu, J. J de chir 28 393, 1926

28 Lamarchia, cited by DaCosta, J. C. Modern Surgery, Philadelphia W. B. Saunders Company, 1931, p. 985

29 Gourrin, V. Des hernies traumatiques de la rate, Thesis, Bordeaux, no 83, 1911

30 Lotsch. Deutsche Ztschr f Chir 93 90, 1908

31 Rieweues, cited by Bier, A., Braun, H., and Kümmell, H. Chirurgische Operationslehre, Leipzig Johann Ambrosius Barth, 1912-1913

CASE 24—A 6 year old boy was struck by an automobile half an hour before admission to the hospital, on Dec 7, 1935. He was not unconscious and complained of abdominal pain. Physical examination gave negative results except for tenderness in the left lower quadrant of the abdomen. The temperature was 97.6 F, the pulse rate 80 and the respiratory rate 24. The urine was normal. The erythrocyte count was 4,000,000 and the leukocyte count 23,600 per cubic millimeter. The value for hemoglobin was 80 per cent while the patient was under observation. On admission, rupture of viscera was suspected. An abdominal and a spinal tap gave negative results. Roentgenograms of the knee and ribs were normal. A roentgenogram of the chest showed broadening of the shadow of the left side of the diaphragm, suggesting the possibility of subphrenic injury. Because of evidence of concealed hemorrhage, operation was deemed advisable. Operation showed the spleen to be enlarged but not lacerated, and there was a small amount of blood in the abdomen. The wound was closed. Twenty-four hours later the patient died. Prior to death the pulse became rapid and thready. Postmortem examination revealed a laceration of the capsule of the spleen 6.2 cm long and 0.64 cm wide across the hilus.

The prognosis for this condition depends not only on the severity of the rupture but on the associated lesions. In the present series of 30 cases, 13 patients died. The gross mortality was 43.3 per cent.

Although every effort should be made to organize a surgical service for rapid diagnosis, it requires about two hours on the average to make a diagnosis of rupture of the spleen. Patients who die within two hours after first being seen by a physician may be considered to have been beyond operative help. We had 5 such patients. In only 83.5 per cent of cases, therefore, could the condition be classed as operable. We know that this is an arbitrary division, but it is the least open to attack, for the severity of splenic laceration or of the associated lesions leaves too much to the personal equation to be satisfactory as a criterion of operability. As long as a positive diagnosis could be made, any of our patients who were operated on were considered suitable, no matter how desperate their condition. Twenty-three operations were performed, 22 splenectomies and 1 exploratory laparotomy. Six of the patients died, a gross operative mortality of 27.3 per cent. Only 5 splenectomized patients died. The operative mortality for splenectomy for traumatic rupture of the spleen in our series was 22.7 per cent. This figure compares favorably with the results reported in the literature. However, we hope to reduce the mortality for rapid diagnosis with the freer use of the abdominal tap, the establishment of the "blood bank" and the maintenance of proper water balance. Table 12 summarizes the 7 cases in which the patients died without operation. In 2 of the cases the diagnosis was missed, although in 1 of these there was evidence of intra-abdominal hemorrhage. The evidence was disregarded. Both patients had severe associated lesions but did not receive the attention they deserved. Five patients

moribund on admission and died within two hours. The diagnosis of intra-abdominal complications was made, but not in time to be of benefit to the patient. In 1 case (case 24) there was a subcapsular hematoma. Exploratory laparotomy was done and the spleen left in situ. The spleen later ruptured. Because of this experience we feel that splenectomy should be done in all cases of traumatic splenic damage.

TABLE 11—*Comparison of Mortality of Splenectomy for Traumatic Rupture of the Spleen*

Author	Number of Splenectomies	Mortality Percentage
McIndoe	37	2.0
Hagen	57	4.9
Lotich	175	5.7
Plansson	140	5.1
Johnson	117	20.0
Connors	25	40.0
Present series	22	2.7

TABLE 12—*Summary of Seven Cases in Which Death Occurred*

Case No.	Associated Lesions	Time in Hospital	Diagnosis
11	Compound fracture of left tibia and fibula fracture of left humerus left ribs shock cerebral concussion shock	2 hr	Made
15	Fractured left ribs shock	1 1/2 hr	Made
14	Shock fractured humerus	1 hr	Made
13	Shock lacerated liver	1 hr	Made
4	Crushed chest lacerated lung and kidney hemothorax hemorrage into galea	1 hr	Made
1	Compound fracture of left tibia and fibula fracture of left humerus fracture of left lower ribs shock lacerated diaphragm lacerated left kidney	6 hr	Missed
8	Lacerated kidney and liver hemothorax subarachnoid hemorrage	4 days	Missed

TABLE 13—*Causes of Death*

Case No.	Diagnosis	Associated Lesions	Time Before Operation	Cause of Death
19	Missed	None	24 hr	Shock
2	Made	Fracture of left tibia left humerus and ribs lacerated lung and kidney shock	24 hr	Shock
3	Made	Fractured ribs	6 hr	Peritonitis
17	Made	Hemothorax mediastinal shift	2 hr	Pulmonary hemorrage
5	Made	Compound fracture of right humerus shock ruptured bladder	2 hr	Shock

Twenty-two splenectomies were done, 5 of the patients died. In table 13 are outlined the causes of death.

In the first case the diagnosis was missed. This case (case 19) has been reported. The patient in case 2 had severe associated lesions and died in shock. The patient in case 3 died of peritonitis on the eighth postoperative day. Postmortem examination revealed generalized

peritonitis, thrombosis of the splenic vein, the portal vein and the pulmonary artery and lobar pneumonia. The death in case 17 was due to an oversight. The diagnosis was made, but a roentgenogram of the chest, taken preoperatively, was reported as normal. However, review of the roentgenogram showed a mediastinal shift and hemopneumothorax. The patient had general anesthesia and died at the conclusion of the operation from a pulmonary hemorrhage. In case 5 not only a splenectomy but a cystostomy was performed. The condition of this patient was very poor, and the two major surgical procedures were more than she could stand.

It will be noted that all but 1 of these patients had associated lesions and were operated on within a reasonable time after admission. The only exception was the patient in whose case the diagnosis was missed. The postoperative complications are enumerated in table 14.

TABLE 14—Postoperative Complications

Case No	Peritonitis	Pulmonary Complications	Pleuritic Reactions	Infection of Wound	Rupture of Wound
16			1	1	
10		1	1		
12		1	1	1	
6				1	
7				1	
9	1				1
3		1	1		
23				1	
26				1	

In summation, 1 patient had postoperative peritonitis and pneumonia, from which he died. Four patients had traumatic pleurisy at the base of the left lung, in the case of 1 of these the pleurisy was evident before operation. Four patients had infected wounds, while only 1 suffered a rupture of the wound. Connors¹ and Bailey³² drew attention to disruption of the wound as being possibly due to trauma to the pancreas. Cases, however, have been reported in which the pancreas was injured at operation without subsequent infection of the wound. Peritonitis following splenectomy was believed not to occur.³³ However, this complication is always possible when the peritoneal cavity is opened.

Splenectomy has been shown to have no ill effect on the organism. This may be due to (1) assumption of the functions of the spleen by the reticuloendothelial system, (2) hypertrophy of accessory spleens or (3) splenic implants.

The spleen is a part of the reticuloendothelial system, and it is only natural that in its absence the remainder of the system assumes its functions.

32 Bailey, H. Brit J Surg 15 40, 1928
33 Hubbard, C. C. New York M J 30 75, 1879. Ledderhose

Accessory spleens are more common than is believed. Curtis and White³⁴ concluded that accessory spleens occur in 10 per cent of cases in which autopsy is performed. In the course of 35 splenectomies they observed accessory spleens in 7 instances. Morrison, Lederer and Fradkin³⁵ found that in 35 per cent of autopsies accessory spleens were observed. They also showed that such organs are most common in infancy and tend to disappear with age. Enlargement of accessory spleens to the size of a normal spleen after splenectomy for rupture of the spleen has been noted.

Eccles and Freer³⁶ reported the case of a man aged 21 who suffered a rupture of the spleen while playing football. Splenectomy was done. Ten years later the patient was reoperated on for ventral hernia, and a normal-sized accessory spleen was found in the splenic bed.

The locations of accessory spleens have been listed by Schilling³⁷ in the descending order of their frequency: at the splenic hilus, in the gastrosplenic omentum, in the greater omentum, along the edge of the omentum, in the splenocolic ligament, in the pleurocolic ligament and in the peritoneal tissues about the splenic venules along the pancreas. In addition, they have been reported as occurring on the intestinal wall, in the mesentery, on the greater curvature of the stomach, on the transverse colon, in the liver, in the scrotum and in the pouch of Douglas.

Finally, splenic implants may take over the function of the lost spleen. Shaw and Shafi³⁸ reported the case of an Egyptian man aged 20 on whom splenectomy was done some years prior to his death from cardiovascular renal disease. Autopsy revealed eighty-two splenic transplants, eighty being in the peritoneal cavity, scattered over the diaphragm, the great omentum and the pouch of Douglas, one in the left pleural cavity, on the lateral aspect of the centrum of the eighth dorsal vertebra, and the last embedded in the left margin of the liver, just beneath the capsule. Three nodules were either pedunculated or sessile, were dark red and varied from 0.2 to 2 cm.

Lee³⁹ described a case in which he operated for intestinal obstruction. Fifteen years previously, a splenectomy had been done for traumatic rupture of the spleen. The peritoneal cavity was studded with greenish black tumors, sessile and pedunculated, ranging from the size of a pinhead to 1 by $\frac{1}{2}$ inch (2.5 by 1.2 cm). Biopsy showed that

34 Curtis, G, and White, P. *Tr West S. A.* **46** 364, 1937.

35 Morrison, M., Lederer, M., and Fradkin, W. *Am J M Sc* **176** 672, 1928.

36 Eccles, W., and Freer, G. *Brit. M J* **2** 515, 1921.

37 Schilling, K. *Virchows Arch f path Anat* **188** 65, 1907.

38 Shaw, A. and Shafi, A. *J Path & Bact* **45** 215, 1937.

39 Lee, R. T. *Lancet* **1** 1312, 1923.

TABLE 15—Summary of Thirty Cases of Traumatic Splenic Rupture

Case No	Date Admitted	Date Discharged	Age, Sex	History	Abdominal Examination	Associated Conditions	Results of Abdominal Tap	Laboratory Data	Pre-operative Diagnosis	Operation	Result
1	3/26/33	3/27/33	♂ 43	Struck by automobile	Generalized tenderness and spasm, marked in left upper quadrant	Compound fracture left tibia, left fibula, fracture left humerus, left lower ribs, ruptured kidney and diaphragm, shock	Positive	Urine bloody R.B.C., 1,800,000 W.B.C., 8,200 Hemoglobin, 85%	Missed	None	Died
2	7/28/32	7/28/32	♂ 20	Struck by automobile	Generalized tenderness and spasm, marked in left upper abdominal quadrant	Fractured left tibia, left humerus, left ribs, lacerated lung and kidney, shock	Positive	Urine bloody R.B.C., 3,500,000 W.B.C., 12,200	Made	Splenectomy	Died
3	7/18/32	5/16/32	♂ 20	Struck by automobile	Generalized tenderness and rigidity	Fractured ribs	Negative	Urine normal R.B.C., 1,000,000 Hemoglobin, 63%	Made	None	Died
4	1/12/31	4/12/31	♂ 40	Struck by automobile	Upper part of abdomen rigid and tender shifting dullness	Crushed chest, lacerated lung and kidney, hemo thorax, hemorrhage into galea		Urine bloody		Splenectomy, cystostomy	Died
5	9/20/31	9/20/31	♀ 27	Fall from window	Soft distention right side	Compound fracture of right humerus, shock, ruptured urinary bladder		R.B.C., 3,500,000 Hemoglobin, 60% Urine could not be obtained	Made	Splenectomy	Cured
6	9/20/31	9/20/31	♂ 8	Struck by automobile	Generalized tenderness and rigidity	Fractured ribs, dis located clavicle	Positive	Urine normal R.B.C., 4,200,000 Hemoglobin, 70%	Made	Splenectomy	Cured
7	11/15/30	11/15/30	♀ 3	Struck by automobile	Tenderness appeared 24 hours after injury spasm in left upper quadrant	Fractured ribs and left femur, hemothorax, sub lacerated kidney and liver, hemothorax, arachnoid hemorrhage	Positive	Urine normal R.B.C., 4,100,000 Hemoglobin, 75%	Missed	None	Died
8	11/15/30	11/15/30	♂ 25	Struck by automobile	Spasm in left upper quadrant	Fractured skull left tibia left fibula	Negative	Urine bloody	Made	Splenectomy	Cured
9	10/11/31	11/11/31	♂ 12	Struck by automobile	Tenderness appeared 24 hours after injury spasm in left upper quadrant		Positive				
10	11/15/30	11/15/30	♂ 12	Struck by automobile	Tenderness appeared 24 hours after injury spasm in left upper quadrant		Positive				

TABLE 15—Summary of Thirty Cases of Traumatic Splenic Rupture—Continued

Case No	Date Admitted	Date Discharged	Sex	Age, Years	History	Abdominal Examination	Associated Conditions	Results of Abdominal Tap	Laboratory Data	Pre operative Diagnosis	Operation	Result
21	2/2/33	3/11/33	♂	10	Fell to curbstone	Tenderness and spasm in lower part of abdomen shifting dullness			Urine normal R B C, 3,900,000 W B C, 23,000 Hemoglobin, 65%	Made	Splenectomy	Cured
						Tenderness and spasm in lower part of abdomen shifting dullness		Positive	Urine normal R B C, 4,450,000 W B C, 11,200	Made	Splenectomy	Cured
						Tenderness and spasm over right side			Urine normal	Missed	Exploratory laparotomy	Died
						Generalized tenderness and spasm		Negative	Urine normal R B C, 4,000,000 W B C, 23,000 Hemoglobin, 80%	Made	Splenectomy	Cured
22	7/30/32	8/27/32	♂	23	Fall from window	Epigastric pain, nausea and vomiting			Urine normal R B C, 4,800,000 W B C, 7,800 Hemoglobin, 82%	Made	Splenectomy	Cured
23	3/31/33	5/9/33	♂	47	Struck by automobile	Tenderness in both upper abdominal quadrants		Positive	Urine normal R B C, 4,900,000 W B C, 10,000 Hemoglobin, 75%	Made	Splenectomy	Cured
24	12/7/35	12/9/35	♂	6	Assault and battery	Tenderness and spasm in upper abdominal quadrants			Urine normal R B C, 4,580,000 W B C, 6,900 Hemoglobin, 65%	Made	Splenectomy	Cured
25	7/11/31	8/1/31	♂	32	Struck by bicycle	Tenderness and spasm in left upper abdominal quadrant			Urine normal R B C, 3,400,000 W B C, 7,800 Hemoglobin, 80%	Made	Splenectomy	Cured
26	9/16/30	10/1/30	♂	11	Assault and battery	Tenderness and spasm in left upper abdominal quadrant		Positive	Urine normal R B C, 4,800,000 W B C, 8,000 Hemoglobin, 70%	Made	Splenectomy	Cured
27	5/16/33	9/1/33	♂	33	Assault and battery	Tenderness and spasm in left upper abdominal quadrant			Urine normal R B C, 4,800,000 W B C, 8,000 Hemoglobin, 70%	Made	Splenectomy	Cured
	1/21/33	2/3/33	♂	17	Collision accident	Abdomen distended spasm in left upper abdominal quadrant			Urine normal R B C, 4,800,000 W B C, 8,000 Hemoglobin, 70%	Made	Splenectomy	Cured
	1/21/33	2/3/33	♂	17	Struck by automobile	Tenderness and spasm in both lower quadrants			Urine normal R B C, 4,800,000 W B C, 8,000 Hemoglobin, 70%	Made	Splenectomy	Cured
	1/21/33	2/3/33	♂	17	Struck by automobile	Tenderness and spasm in both lower quadrants			Urine normal R B C, 4,800,000 W B C, 8,000 Hemoglobin, 70%	Made	Splenectomy	Cured

they were normal splenic tissue. Others have reported similar cases ⁴⁰. In 1 case in which we had the opportunity to reoperate there were no splenic implants.

These implants are believed to originate from autoplasmic transplants from the spleen. To support this view, attention is called to the fact that they appear only in cases in which the spleen has been removed for rupture. Removal of a diseased spleen is rarely, if ever, followed by transplants. Faltin ^{40b} and von Stubenrauch ^{40d} concluded that they develop from spleen-forming rests.

There has been much discussion as to the return of the blood picture to normal after splenectomy for traumatic rupture. Hitzrot ⁴¹ noted anemia, which persisted for a varying period but gradually returned to normal after one to three months. He also noted a change in resistance of the blood cells.

Pfeiffer and Smyth ⁴² have observed cases in which there was definite and persistent anemia. Connors ¹ had the opportunity to observe a splenectomized patient in whom anemia persisted for seventeen years. Others have stated that anemia disappears about two months after operation ⁴³.

The effects of splenectomy on the blood platelets were studied by Rosenthal ⁴⁴ and others, ⁴⁵ who noted that there is a gradual and constant increase in the number of blood platelets, reaching its zenith during the second week. Platelet counts of 1,000,000 to 1,900,000 were observed. The platelet count begins to drop and becomes normal, or remains somewhat above normal, about the third or fourth week after operation. Observation in these cases for five years after operation has shown the platelet count to be normal or slightly above normal.

Other mentioned results of splenectomy for traumatic rupture of the spleen are hyperplasia of the peripheral lymph glands, hyperplasia of the marrow of the long bones, increase in weight, increase in appetite and decreased resistance to infection. Severe or late effects on the health and well-being of the splenectomized person are negligible or absent.

A resume of our cases is presented in table 15.

40 (a) Kupperman, W. *Zentralbl f Chir* 63 3061, 1936. (b) Faltin, R. *Deutsche Ztschr f Chir* 110 160 1911. (c) Kuttner. *Verhandl d deutsch Gesellsch f Chir* 36 25 1907. (d) von Stubenrauch. *ibid* 42 213, 1912. (e) Smyth, C M, Jr. *S Clin North America* 9 1181, 1929.

41 Hitzrot J M. *Ann Surg* 67 540 1918.

42 Pfeiffer D B and Smyth, C M Jr. *Ann Surg* 80 562, 1924. Smyth ^{40e}.

43 Boyd, W. *Surgical Pathology*, Philadelphia, W B Saunders Company 1925 p 591. Angle and Kassel ⁴.

44 Rosenthal, N, cited by Connors ¹.

45 Shore B R and Kreidel, K U. *Ann Surg* 99 307 1934.

SUMMARY AND CONCLUSIONS

Subcutaneous rupture of the normal spleen is more common than is generally believed. In this hospital the condition occurred in 47.6 per cent of cases in which there was subcutaneous injury to the abdominal cavity.

There is no such clinical entity as spontaneous rupture of the normal spleen. The term should be discarded. Except for torsion with rupture, the condition in all cases is due to trauma.

A classification based on the rate of hemorrhage is submitted. The abdominal tap is invaluable as a diagnostic procedure and should be repeated when necessary.

The differential diagnosis must exclude lesions above the diaphragm and retroperitoneal as well as intra-abdominal conditions. The diagnosis is most frequently missed because a history of trauma is not obtained or, if one is obtained, it is disregarded. Associated lesions may mask the signs and symptoms associated with a ruptured spleen.

The treatment of choice. Preoperative rupture of the normal spleen is the operation of choice. Preoperative enemas are forbidden.

The mortality for subcutaneous rupture of the normal spleen is discussed. This mortality can be lowered by (a) constant alertness on the part of the surgeon and the staff to avoid errors in diagnosis, (b) more rapid diagnosis so that the patient will receive the benefits of operation sooner, (c) use of a slow blood drip preoperatively with or without intravenous administration of fluids (when blood from a "bank" is not readily available, infusions of a saline solution should be given), and (d) administration of adequate fluids should be given to restore water balance.

CORRELATION OF PATHOLOGIC AND CLINICAL OBSERVATIONS IN CHRONIC LYMPHOID APPENDICITIS

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A correlation seems to exist between the pathologic diagnosis of a specific type of chronic appendicitis, namely, the chronic lymphoid, and a definite symptom complex, which is herein described. The pathologic changes consist of hyperplasia of the lymphoid elements and a variable degree of fibrosis and obliteration. The clinical picture is characterized by attacks of mild to moderately severe abdominal pain, with a high incidence of nausea and occasional associated episodes of vomiting, recurring over a period lasting from months to years and never being severe enough to fall into the category of acute appendicitis.

Many appendectomies have been performed on the basis of this symptom complex, after careful exclusion, by physical examination and laboratory aid, of other pathologic lesions. In my experience such operations have often revealed relatively innocuous-appearing appendixes. This paper attempts to correlate the gross and microscopic changes in such organs with clinical findings.

Beluffi¹ in 1936 described this pathologic-clinical correlation and thoroughly dealt with the historical and bibliographic aspects of the entity up to that date. His report is based almost entirely on the histologic changes in the appendixes of 100 patients whose illness was diagnosed clinically as chronic appendicitis. He divides these changes into three fundamental types: the hypertrophic-hyperplastic, the sclerotic-atrophic and the obliterative. He considers these three types as "evolutionary stages of the same anatomical-pathological process, of which the initial lesion would be the lymphatic hypertrophy and hyperplasia, the second, an increase of the interstitial connective tissue arriving at sclerosis, the last, the complete closing of the organ." It seemed desirable to emphasize the clinical importance of the syndrome, in addition to corroborating most of Beluffi's pathologic description.

The present pathologic-clinical study is based on all the cases listed as instances of chronic lymphoid appendicitis in the files of the depart-

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1 Beluffi, E. L. *Contributo all'anatomica patologica dell'appendicite cronica*, Arch ital di anat e istol pat 7 226 1936

ment of surgical pathology of the New York Hospital from September 1932 to November 1938. There were 132 uncomplicated cases, in which at operation no other obvious abdominal lesion was presented. In these simple appendectomy was done. There were 50 additional cases in which the appendix was removed incidentally at the time of some other intra-abdominal operation.

MACROSCOPIC PATHOLOGIC OBSERVATIONS

The macroscopic appearance of appendixes removed from patients with chronic lymphoid appendicitis is quite variable. They measure from 4 to 12 cm in length and from 0.6 to 1 cm in diameter. They may be terete, fusiform, cylindric or clavate at the distal end. The tip is clubbed, a bandlike constriction is frequently found just proximal to this. These organs are usually plump and well rounded, and palpation reveals a moderate degree of tensesness. Hyperemia is never an important feature, although a few of the serosal vessels may be minimally injected. The color ranges from light yellowish brown to dark red and moderately deep purple. The serosal surface is generally glistening and smooth, although occasionally there may be evidences of filmy adhesions on the antimesenteric surface, especially near the middle of the appendage. When such adhesions or Jackson's membrane are encountered, there is a tendency for the organ to be slightly bent on itself, forming either a J or an S, while the rarest form is that of an O, with the tip and the base in close proximity. The last is caused by a thickened, short mesentery.

As one transversely sections the organ near the tip, the mucosa in the hypertrophic and in the sclerotic type prolapses markedly, whereas in the obliterative type the central fibrous tissue extrudes. Semitormented soft feces are often expressed when the lumen is patent. Oxyurids were found in 2 specimens in this series, accompanied in 1 instance by a thin sliver of glass, measuring 8 mm in length.

When the appendix is opened longitudinally, a small amount of pasty feces may be present, but fecaliths are rarely found. The mucosa is usually light brown or pink and is often roughly corrugated. There may be occasional petechial hemorrhages in the middle or distal third. Erosions, ulcerations or gross blood are rarely present. The lumen at the point of amputation is small in caliber but approximately 1 meter distally it is often dilated, usually to the tip, unless there is a clubbed end. In that case a concomitant constriction of the lumen at the surface is noted at the proximal end of the swollen tip. Oxyurids show almost no lumen and are fibrosed to the point of obliteration in the distal quarter.

MICROSCOPIC PATHOLOGIC OBSERVATIONS

The present microscopic description closely follows Beluffi's classification. Since the evolutionary stages of chronic lymphoid appendicitis were described by Beluffi, the attention of this department has been focused on this entity, and all of our sections have been reclassified according to the three types previously mentioned.

Hypertrophic-Hyperplastic Type—Microscopic examination of a longitudinal section through an appendix with changes characteristic of the hypertrophic-hyperplastic type of chronic lymphoid appendicitis shows the mucosa to be largely intact. The glandular structures may be atrophic or completely absent. If present, they may appear to be rounded, stratified, and from two to four layers in thickness. The presence of any stratification, however, should be considered an artefact, because in such cases the section is not strictly radial. Throughout the length of the organ there is a wide continuous band of lymphoid tissue, composed of many discrete hypertrophied follicles, with edematous centers and conspicuous marginal sinuses, surrounded by a stroma densely packed with lymphocytes. The muscularis mucosa is indistinct. The lymphoid tissue may invade the submucosa to a moderate degree. The muscularis is normal. Considerable numbers of eosinophils are found scattered throughout the various layers in many cases. These are interpreted as confirmatory evidence of chronicity. Swollen capillaries are noted in each layer, and almost all of them are engorged with red blood cells (fig 1).

Microscopic examination of a cross section near the tip, in an organ typical of the hyperplastic type, shows the mucosa to be intact. The glands are sparse and may or may not contain mucus-secreting cells. Most of them are small, atrophic and compressed by the neighboring overgrowth of follicles and lymphoid tissue. This lymphatic overgrowth occupies from one half to two thirds of the total surface of the appendix.

Sclerotic-Atrophic Type—In this type of appendicitis the mucosa is also intact. Immediately subjacent to this there are one or two layers of small glands which are flattened in a longitudinal direction. Goblet cells are rare. Lymphoid follicles can still be distinguished, although they are seen to be fused with the surrounding lymphoid tissue. They have compact cellular centers and the marginal sinuses are absent. The continuous wide band of lymphoid tissue, typical of the hyperplastic variety, is, in this type, broken up and compressed by the projection into it of dense connective tissue from the submucosa. Thick sclerotic vessels traverse the submucosa. Scar tissue radiates peripherally from it to intersect the muscularis. This sclerosis is evidence of previous inflammatory insults (fig 2).

Obliterative Type—Obliterative appendicitis presents its most characteristic picture on transection. The lumen near the tip is entirely replaced by a continuation centralward of the fibrous connective tissue of the submucosa, which also extends peripherally to interrupt the continuity of the muscularis. A few fibroblasts and lymphocytes are noted in the sclerotic central core. Examination of a longitudinal section may reveal that the lumen is patent from the base of the organ to the distal quarter. Along the patent portion the microscopic observations

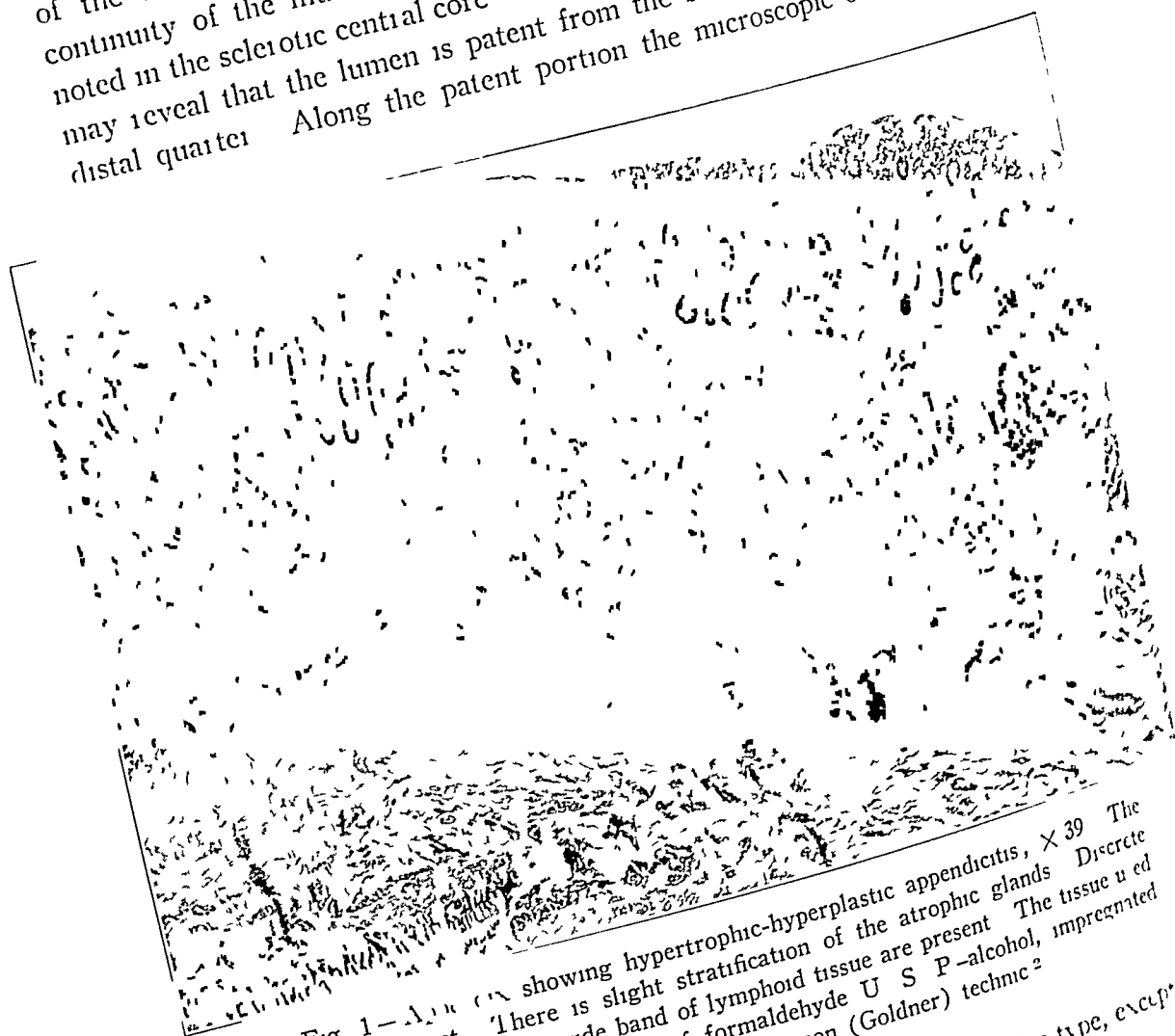


Fig 1—Appendix showing hypertrophic-hyperplastic appendicitis, $\times 39$. The mucosa is intact. There is slight stratification of the atrophic glands. Discrete lymphoid follicles and a wide band of lymphoid tissue are present. The tissue used for study was fixed in solution of formaldehyde U S P—alcohol, impregnated with paraffin and stained with a modified Masson (Goldner) technique.²

resemble those of the previously described sclerotic-atrophic type, except that there is a complete absence of lymphoid tissue.

Polymorphonuclear leukocytes, as a rule, are absent in each of the three types, although occasional appendices may show a superimposed moderately acute flare-up. The nerve plexuses of Auerbach and Meissner are not remarkable in this series. The same is true of

² Goldner, J. A Modification of the Masson Trichrome Technique for Routine Laboratory Purposes, *Am J Path* 14 237, 1938.

subserosa and serosa except that the latter in a few instances shows the presence of filmy adhesions. In rare cases the lymphatic spaces contain numerous leukocytes, including polymorphonuclears, but these are not widely distributed throughout the tissue.

By way of comparison, the chronic ulcerative type of appendicitis will be described. In this the mucosa is irregular and contains numerous minimal erosions and ulcerations along its surface (fig 3). Each of these is surrounded by a zone of lymphocytes and polymorphonuclear leukocytes. Lymphoid tissue is present in diminished amount, or it

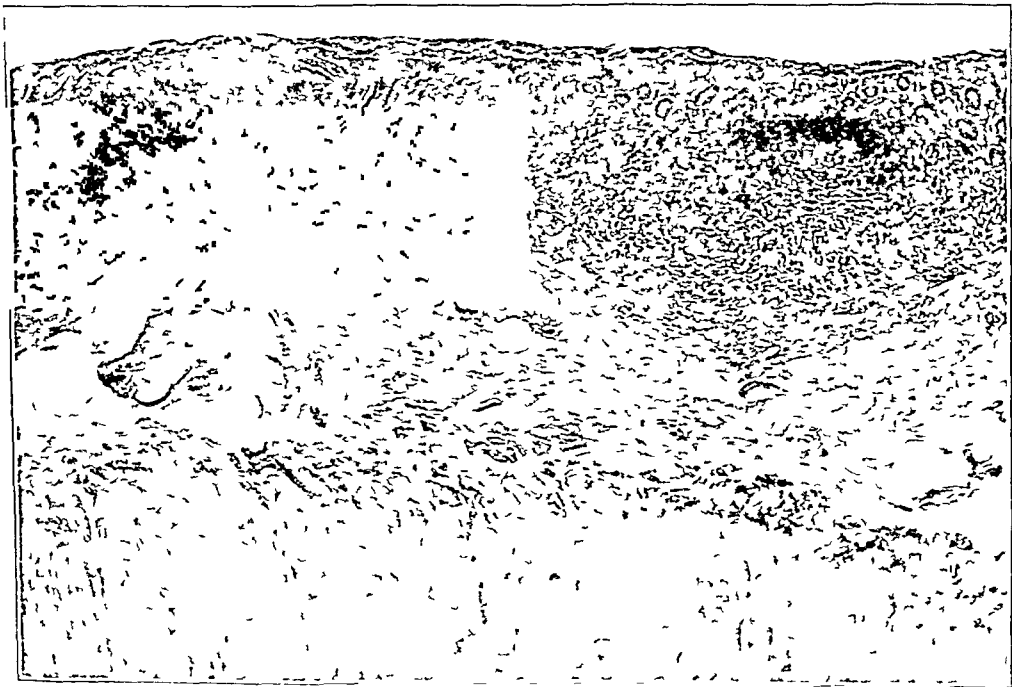


Fig 2—Appendix showing sclerotic-atrophic appendicitis, $\times 39$. The glands are flattened beneath the intact mucosa. The lymphoid follicles are fused. The lymphoid tissue is diminished in amount as compared with a similar field in figure 1.

may be entirely wanting. The blood vessels are increased in number and are dilated. Many leukocytes, particularly polymorphonuclear leukocytes, are noted in the mucosa, submucosa and muscularis. There is a definite increase in the fibrous connective tissue of the submucosa, which also is likely to be heavily infiltrated with fat cells. The muscularis is hypertrophied and crossed by fibrous connective tissue strands. Auerbach's plexuses are hyperplastic and may contain atypical ganglion cells. The serosa is usually very greatly thickened. In short, chronic ulcerative appendicitis shows pathologic changes in every layer, whereas in

chronic lymphoid appendicitis abnormalities are confined largely to the mucosa and submucosa. Both this and the sclerotic-atrophic type lead ultimately to fibrous obliteration of the lumen.

CLINICAL OBSERVATIONS

Of the 132 patients with uncomplicated chronic lymphoid appendicitis 48 were males and 84 females. Nausea was present in 60 per cent, nausea and vomiting combined, in 30 per cent, 2 patients induced

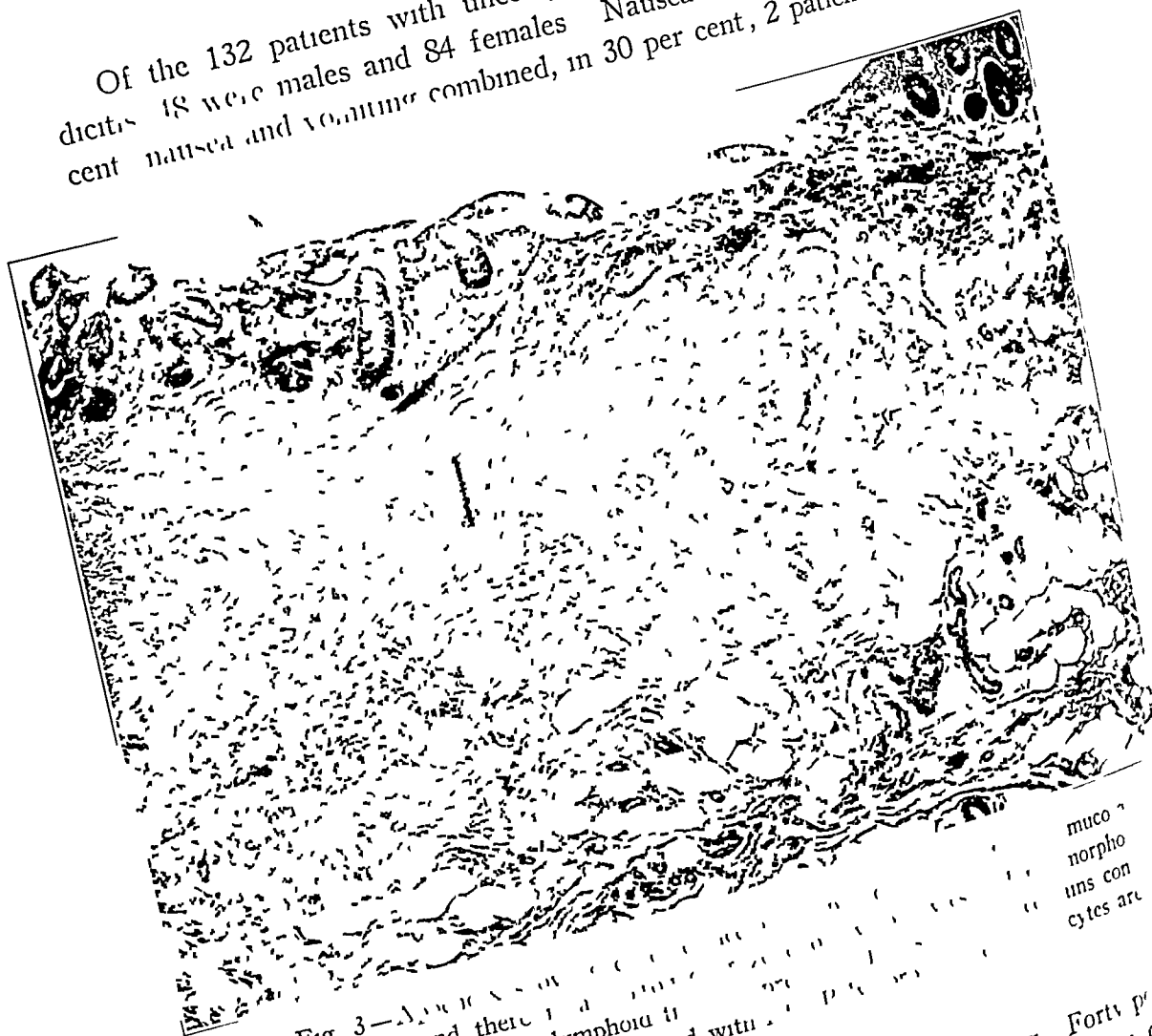


Fig 3—Appendix is ulcerated, and there are nuclear leukocytes. No lymphoid tissue is seen in each layer.

vomiting, and 1 patient vomited during spasms of coughing. Forty per cent had neither nausea nor vomiting. The percental distribution of appendectomies according to decades of life was as follows: 1 to 10, 11 per cent, 11 to 20, 39 per cent, 21 to 30, 25 per cent, 31 to 40, 20 per cent, 41 to 50, 35 per cent, 51 to 60, 15 per cent. Since there is a physiologic hyperplasia of the lymphoid elements in children and adolescents, the appendixes removed in the first two decades may be interpreted as not abnormal except that in these organs occur

the largest percentage with mild infiltration by polymorphonuclear leukocytes. One patient in this group had an appendical abscess drained one year before appendectomy, but on microscopic examination, interestingly enough, there was no pathologic change except lymphoid hyperplasia.

One of the striking features of this study is that 66 of the 132 patients gave a history of recurring attacks of pain in the right lower quadrant of the abdomen over a period of from one to ten years. Many of these patients used the words "several years" in describing the duration of symptoms attributable to chronic appendicitis. Of the remaining 66 patients, 24 complained of similar symptoms for from one to several months, whereas 42 noted abdominal distress over a period of from a

TABLE 1—*Location of Abdominal Pain*

Location	Cases	
	Number	Per Cent
Right lower abdominal	77	58
Generalized abdominal	25	38
Epigastric	16	
Umbilical	7	
Right and left lower abdominal	5	4
None	4	

TABLE 2—*Examining Surgeon's Interpretation of Abdominal Tenderness and Muscle Spasm*

	Tenderness			Rebound	None	Muscle Spasm
	Slight	Moderate	Acute			
Cases	40	46	4	10	20	12
Percentage	30	35	3	8	15	9

few hours to three weeks. The percentage in whom abdominal pain originated and remained in the right lower quadrant and at McBurney's point was 58, patients with vague abdominal, epigastric and umbilical distress localizing in the right lower quadrant constituted another 38 per cent, the other 4 per cent had either mild discomfort in both lower quadrants of the abdomen or no localized pain (table 1).

On palpation of the abdomen 71 per cent of the patients complained of discomfort in the right lower quadrant or at McBurney's point, 14 per cent had tenderness at the umbilicus or in both lower abdominal quadrants, and 15 per cent had none at any location.

Since a major operation was contemplated, it is significant to note that tenderness interpreted by the surgeon, was acute in but 3 per cent, moderate in 34 per cent, and slight in 50 per cent. In addition to discomfort, 9 per cent had spasm of the right rectus or obliquus muscles and 8 per cent had rebound tenderness referred to McBurney's point. The remainder, or 15 per cent, had no distress, as indicated in table 2.

The preoperative temperatures of these patients averaged 37 C (98.6 F), with some slightly subnormal and others a few tenths of a degree above normal. Further evidence of the chronic nature of this disease is found in the study of the white blood cell counts. In 55 per cent of the cases the leukocytes numbered from 5,000 to 10,000, in 42 per cent from 10,000 to 15,000 and in 3 per cent more than 15,000 per cubic millimeter.

No study has been made regarding the follow-up on the patients, since many were on the Private Pavilion and there are no available data. Data on those who have been operated on within the last year

TABLE 3—Cases in Which Incidental Appendectomies Were Performed

Operation	Cases		
	Number	Per Cent	
Gastroenterostomy	3	6	Hysterectomy Uterine ventral suspension Oophorectomy Salpingectomy Operation for bleeding granular follicle Dilatation and curettage
Cholecystectomy	20	40	
Operation on female generative organs	20	40	
Resection of ascending colon for carcinoma of cecum	1	2	
Operation for mesenteric adenitis	3	6	
Removal of Meckel's diverticulum	1	2	
Operation for terminal ileitis	1	2	
Higgin's bilateral ureteral transplant	1	2	

TABLE 4—Data on Five Complicated Cases in Which Variations from the Average White Cell Count and the Average Temperature in Uncomplicated Cases Were Found

Temperature	Lesion	Leukocytes per Mm
38.4 C (101.1 F)	Mesenteric adenitis	20,400
38.4 C (101.1 F)	Salpingitis	16,000
37.6 C (99.6 F)	Salpingitis	26,000
38.2 C (100.7 F)	Bleeding granular follicle	10,000
37.0 C (98.6 F)	Cholecystitis	21,600

also cannot be of value from this standpoint. There were few complications. One patient had a wound infection requiring drainage. Two patients had unexplained fever of 39 C (102.2 F) or more, and another had leukocytosis (white cell count above 15,000) during the entire week after operation. All these recovered. There were no deaths. Those cases in which an incidental appendectomy was done during the course of another intra-abdominal operation total 50 and are classified as cases of asymptomatic pathologic conditions of the appendix. These are listed in table 3.

One is reluctant to exclude a number of these cases, in which gastrointestinal symptoms were a feature for many years, from the group of the symptom complex of chronic appendicitis, since many of the terminal patients were found to have pathologic changes in the generative organs.

at operation, such as bleeding graafian follicles, ovarian cysts and retroverted uteri. An analysis of the findings in this group closely parallels those in the uncomplicated group. There were 12 males and 38 females. Nausea occurred in 44 per cent, vomiting in 26 per cent, and neither in 56 per cent. The white cell counts and temperatures varied from the average in the preceding series in 5 instances (table 4).

Operation was performed between the ages of 20 and 50 in 78 per cent of the patients. Sixty-eight per cent had complained of abdominal pain over a period of from one to many years and 14 per cent had noted symptoms for several months. Distress occurred in the right upper quadrant of the abdomen in 30 per cent and in the right lower quadrant in 28 per cent, and umbilical, epigastric or generalized abdominal pain in 28 per cent. A group without abdominal pain included those with menorrhagia, metrorrhagia or sterility. Therefore it seems from the foregoing figures that the symptoms of at least half of these patients could be explained more clearly on the basis of chronic appendicitis than on that of the other operative finding. The latter may in reality, be the incidental finding and chronic appendicitis the primary lesion. It is granted that in such cases biliary tract disease, peptic ulcer, terminal ileitis or Meckel's diverticulum could easily share symptoms with chronic appendicitis.

Chronic lymphoid appendicitis is an apparently definite pathologic and clinical entity which accounts for many cases of "chronic appendicitis" in which the surgeon is disappointed at the comparatively normal-looking organ he has removed, one which is in reality abnormal, as shown in this study.

SUMMARY

The pathologic changes in a specific type of appendicitis, namely, chronic lymphoid appendicitis, have been described.

One hundred and thirty-two cases of chronic lymphoid appendicitis have been analyzed clinically. Symptoms were present for as long as ten years, vomiting occurred in 50 per cent, pain usually focused in the right lower quadrant of the abdomen, spasm of the abdominal muscles and rebound tenderness were rare, the temperature was normal and the leukocyte count ranged between 5,000 and 15,000.

The pathologic diagnosis of chronic lymphoid appendicitis has been found to coincide with the clinical syndrome described.

Fifty incidental appendectomies have been tabulated, and the importance of the appendical lesions has been stressed.

CAPILLARY PERMEABILITY AND INFLAMMATION IN NARCOTIZED RABBITS

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A difference in the response of narcotized and of normal animals has been observed in anaphylactic shock. Besredka¹ found that sensitized guinea pigs which received the shocking reinjection while under ether anesthesia showed no anaphylactic symptoms. Banzhaf and Famulener² obtained similar results with chloral hydrate. Farmer³ recently has shown that ethyl carbamate (urethane) administered to sensitized guinea pigs prior to the shocking reinjection led to the survival of 15 of 30 animals. Besredka explained the action of the narcotic by assuming that the ether "allowed the nerve cell to remain indifferent to the union" of the antigen and antibody. Farmer, however, stated the opinion that this effect of a narcotic is probably attributable to its peripheral action on the bronchial musculature. The exact mechanism by which anesthesia may alter the animal's reaction is apparently not clearly understood.

Dale and Laidlaw⁴ have pointed out that rabbits under ethyl carbamate (urethane) anesthesia fail to show the depressor vasodilator response to small intravenous injections of histamine. Abel and Geiling⁵ observed that capillary dilatation in the skin and mucous membranes was either absent or markedly diminished when dogs were anesthetized with ether before receiving an intravenous injection of albumoses. Krogh⁶ has shown that local anesthesia either partly

From the Departments of Surgery and Pathology, Vanderbilt University
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Sciences of the Rockefeller Foundation

1 Besredka, A. *Commentaire de l'anaphylaxie*. Ann Inst Pasteur **21** 950, 1907

2 Banzhaf, E., and Famulener, L. The Influence of Chloral Hydrate in Serum Anaphylaxis, J Infect Dis **7** 577, 1910

3 Farmer, L. *The Influence of Narcotics on Anaphylactic Shock*, J Immunol **32** 195, 1937

4 Dale, H. H., and Laidlaw, P. P. The Physiological Action of B-aminazol 1 ethylamine, J Physiol **41** 318, 1910

5 Abel, J. J., and Geiling, E. M. K. Some Hitherto Undescribed Properties of the Constituents of Witte's Peptone, J Pharmacol & Exper Therap **23** 1, 1924

6 Krogh, A. The Anatomy and Physiology of the Capillaries, ed 2, New Haven, Conn., Yale University Press, 1929, p 170

or completely inhibits the development of macroscopic evidence of inflammation Hirschfelder⁷ and Langley⁸ failed to confirm this observation Pickrell⁹ recently has stated that alcoholic intoxication maintained at the point of stupor destroys the resistance of rabbits to pneumococcal infection This loss of resistance, according to Pickrell, "appears to be due to the fact that intoxication profoundly inhibits the vascular inflammatory response as long as the intoxication is maintained" Pickrell stated that in the absence of capillary dilatation and of margination of the leukocytes leukocytic emigration at the site of infection is negligible and the bacteria therefore proliferate uninterruptedly Similar experiments show that "ether or avertin anesthesia has as marked an inhibitory effect on the inflammatory response as has alcoholic intoxication, and produces as marked a loss of resistance to infection" The significance of Pickrell's observations if such a process should occur in the human being is obvious

In the present paper the capillary permeability and the inflammatory reaction have been studied in rabbits and mice, the former by observation of the localization and concentration of trypan blue in areas of rabbits' skin treated with xylol and the latter by macroscopic and microscopic observation of skin previously treated by intradermal injections of aleuronat, infusion broth cultures of staphylococci and cultures of *Pneumococcus* type III The anesthetics used in this study were alcohol ether and pentobarbital sodium

EXPERIMENTS

Effect of Anesthesia on the Localization of Trypan Blue in Areas of Inflammation Produced by Xylene—The localization and concentration of trypan blue in areas of inflammation produced by application of xylene to the rabbit's skin has been described by Rigdon¹⁰ The method is as follows The rabbit's skin is carefully shaved twenty-four to forty-eight hours before use Squares of skin are marked out with india ink, and xylene is painted on different areas of the same rabbit with a cotton applicator without rubbing, usually at intervals of ninety, sixty, forty-five, thirty and fifteen minutes and immediately before intravenous injection of 10 cc of 0.2 per cent trypan blue Each side of the animal may be used if duplicate results are desired

7 Hirschfelder, A D Studies upon the Vascular and Capillary Phenomena and Supposed Anon Reflexes Concerned in the Development of Edema in Mustard Oil Conjunctivitis, Together with the Effects of Vasodilator Drugs, Local Anesthetics and Vital Stains, *Am J Physiol* **70** 507, 1924

8 Langley, S N Antidromic Action *J Physiol* **58** 49, 1923

9 Pickrell, K L The Effect of Alcoholic Intoxication and Ether Anesthesia on Resistance to *Pneumococcal* Injection, *Bull Johns Hopkins Hosp* **63** 238, 1938

10 Rigdon, R H Capillary Permeability in the Skin of the Rabbit, to be published

The effect of alcohol, ether and pentobarbital sodium anesthesia on the localization and concentration of trypan blue was studied. Rabbits weighing 2 to 3 Kg were given 60 cc of 20 per cent ethyl alcohol by stomach tube, this usually produced a deep stupor comparable to surgical anesthesia. Additional amounts of alcohol were given during the experiments when indicated. Ether was given by inhalation, the animal being kept under light surgical anesthesia. Pentobarbital sodium was administered intravenously in an initial dose of 30 mg per kilogram of body weight, with the subsequent addition of smaller doses as needed to maintain anesthesia. Pentobarbital gave the lightest anesthesia of the three anesthetics used. The application of xylene was begun after anesthesia had been obtained.

In the normal rabbit, as seen in a large number of animals and as previously described by Rigdon,¹⁰ trypan blue localizes and concentrates in a characteristic fashion in cutaneous areas of inflammation produced by xylene. Within one minute after the dye is given intravenously it can be seen staining the area to which xylene was applied immediately before, and its concentration increases rapidly. Shortly thereafter the dye begins to appear and concentrate in the areas painted with xylene fifteen and thirty minutes before. Occasionally dye first appears in the area painted fifteen minutes before and in one-half to one minute is seen in the area to which xylene was applied immediately before injection. Thirty minutes after the dye is given, a regular gradation of intensity of staining of the painted areas is seen. The area to which xylene was applied immediately before the injection is intensely blue, with progressively less dye in the areas painted fifteen, thirty, forty-five, sixty and ninety minutes before the dye was given. Areas to which xylene has been applied longer than the surrounding skin.

In anesthetized animals the order in which trypan blue localizes is altered. In 5 animals intoxicated with alcohol dye appeared first in the area treated with xylene fifteen minutes before giving the dye, and two to twenty-five minutes later it first could be determined to be present in the area treated immediately before injection of dye. Figure 1 demonstrates the difference between the normal and the alcohol-treated rabbits. The areas were treated with xylene fifteen minutes before, five minutes before and immediately before the dye was given, and the photograph was taken twenty minutes after. The control animal had the greatest amount of dye in the area treated with xylene immediately before, with progressively less in the areas treated five and fifteen minutes before, and the rabbit anesthetized with alcohol had the greatest concentration of dye in the area painted fifteen minutes before, with progressively decreasing amounts in the remaining two areas. The duration of alcoholic intoxication apparently did not influence the alteration in localization and concentration of trypan blue. The reaction was the same in rabbits given the dye one hour after intoxication and in rabbits to which the localization of dye was determined six hours after intoxication. The rabbit anesthetized with ether (3 rabbits) showed the same type of staining in the skin treated with alcohol, with slightly less delay in appearance of the dye. From three to seven minutes before the dye was given the least delay in the localization of dye which appeared immediately before injection of trypan blue. Pentobarbital caused the least delay in the localization of dye which appeared one to two and one-half minutes before and its appearance in the area painted before than in that painted fifteen minutes before. This was of interest in the type and depth of anesthesia.

Inflammation Produced by Xylene, Alcuronat and Bacteria in Anesthetized Animals—Rabbits intoxicated with alcohol as described were used for the study of the inflammatory response. Application of xylene to normal rabbit skin is followed shortly by hyperemia with subsequent edema. At six to eight hours the skin is definitely edematous and slightly red (there is some variation among normal rabbits in the extent and degree of edema). Six rabbits intoxicated with alcohol all demonstrated hyperemia and edema on application of xylene to the skin, which were not noticeably different from the reactions of normal rabbits either immediately or at the end of eight hours, when the animals were killed by a blow on the head and the treated areas were removed for microscopic section.

Microscopic sections of the cutaneous areas treated with xylene in the rabbits given alcohol showed a definite decrease in the number of leukocytes present as

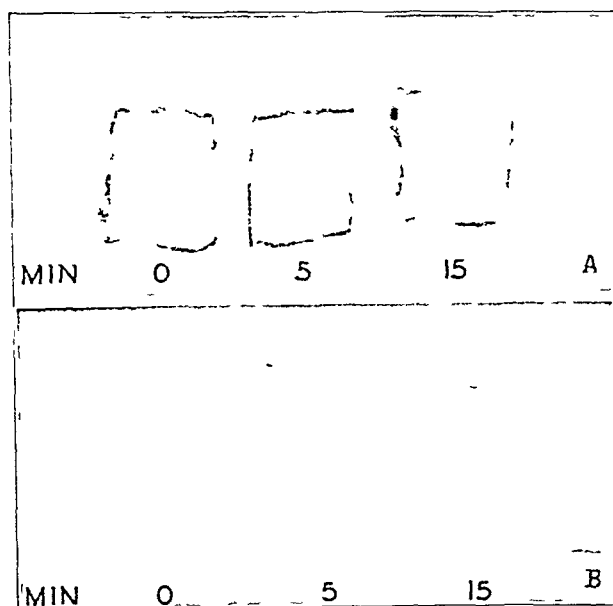


Fig 1—Cutaneous areas of (A) a rabbit intoxicated with alcohol and (B) a nonintoxicated rabbit, treated with xylene fifteen minutes, five minutes and immediately before intravenous injection of 10 cc of trypan blue. The photograph was taken twenty minutes after the dye was given. In A the greatest amount of dye is in the area treated with xylene fifteen minutes before the injection, in B the greatest concentration is in the area treated with xylene immediately before the dye was given.

compared with lesions of similar age in the skin of the normal rabbit. In the xylene-treated skin of the normal rabbit the leukocytes were located primarily in the dermis, with the greatest number adjacent to the epidermis. The leukocytes were present in the lumens and about the peripheries of the small blood vessels. In the anesthetized animals there was absence of leukocytes in the lumens of the small vessels. This fact suggests that some effect was produced in the rabbit which prevented the leukocytes from concentrating in the small vessels rather than that the leukocytes were unable to pass through the vessel wall.

Figure 2 demonstrates the difference in the number of leukocytes in the xylene treated skin after eight hours in an intoxicated and in a control rabbit.

The reaction to aleuronat was observed in a group of 4 rabbits anesthetized with alcohol and in a group of 4 control rabbits. Two-tenths cubic centimeter of a 1 per cent suspension of aleuronat in 0.9 per cent saline solution was injected intradermally into two cutaneous areas in each rabbit. In four hours there was an area of edema 1 cm across, without hyperemia, in both groups. Some hyperemia was present, and a variation between animals in the same group was noted, but on the whole no greater reaction was seen in the control group than in the intoxicated.

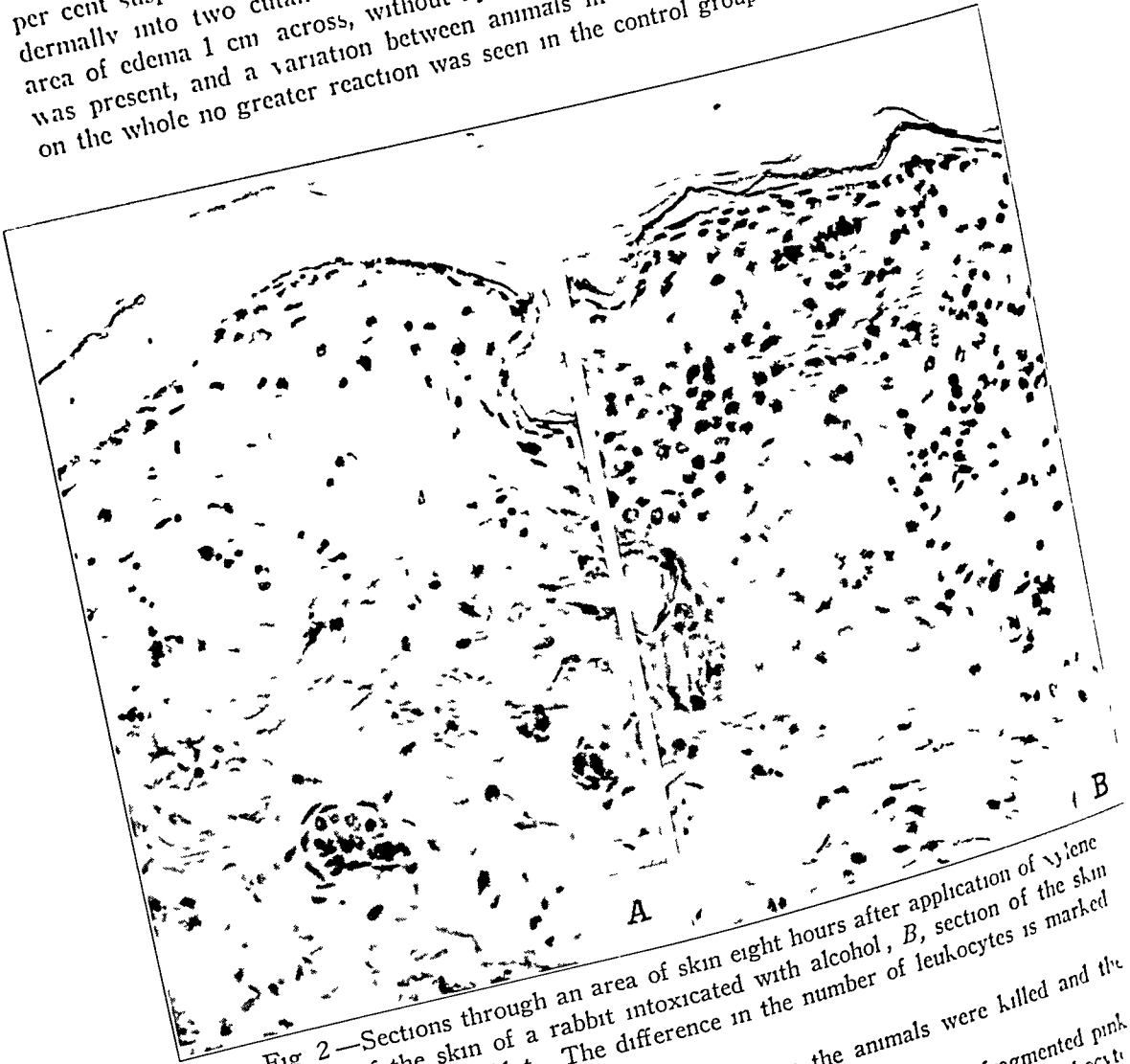


Fig 2—Sections through an area of skin eight hours after application of xylene. A, section of the skin of a rabbit intoxicated with alcohol; B, section of the skin of a nonintoxicated rabbit. The difference in the number of leukocytes is marked.

cated animals at the end of eleven hours, when the animals were killed and the lesions removed for microscopic study.

In sections the aleuronat appeared in the dermis as a mass of fragmented pink staining material. Infiltrating this and the surrounding tissue were leukocytes. The number of leukocytes in the lesions of the normal animals was greater than in those of the intoxicated animals (fig 3).

To determine whether the effect of alcohol on the reaction induced by organic aleuronat was paralleled that induced by xylene and aleuronat, 6 rabbits intoxicated with alcohol were given intradermal injections of 0.5 cc of a broth culture of a nonpathogenic producing *Staphylococcus aureus* and 5 intoxicated rabbits were given injections of 0.2 cc of a culture of *Pneumococcus* type III. Five nonintoxicated rabbits

were similarly inoculated with staphylococci and 5 with pneumococci. In each rabbit the injection was given in two areas. In each of 3 intoxicated rabbits and in 1 nonintoxicated rabbit staphylococci and pneumococci were injected on opposite sides for comparison.

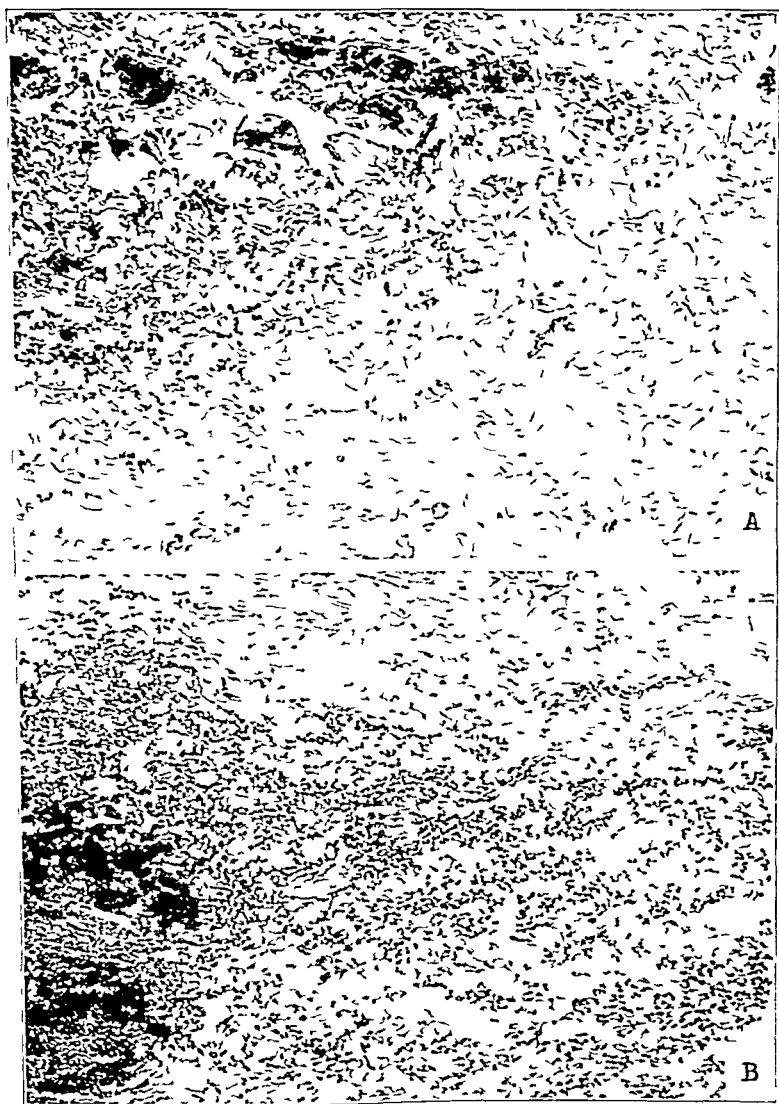


Fig. 3—Section through the skin into which aleuronat was injected, after eleven hours. *A*, skin from a rabbit intoxicated with alcohol. *B*, skin from a nonintoxicated rabbit. The difference in the number of leukocytes about the mass of aleuronat is evident.

In the nonintoxicated animals after six hours all the areas inoculated with organisms showed hyperemia and edema which in some were moderate and in

others intense. A few of the intoxicated rabbits, both with staphylococci and with pneumococci, showed a very slight or a barely perceptible reaction at the site of inoculation, but some showed a moderate amount of hyperemia and edema, as great as that observed in some of the nonintoxicated group. In the same animal pneumococci and staphylococci gave parallel reactions, that is, both gave slight reactions or both gave moderate reactions. On the whole, the nonintoxicated rabbits showed more severe gross lesions than did the intoxicated rabbits. The animals were killed after six hours for microscopic study of the lesions.

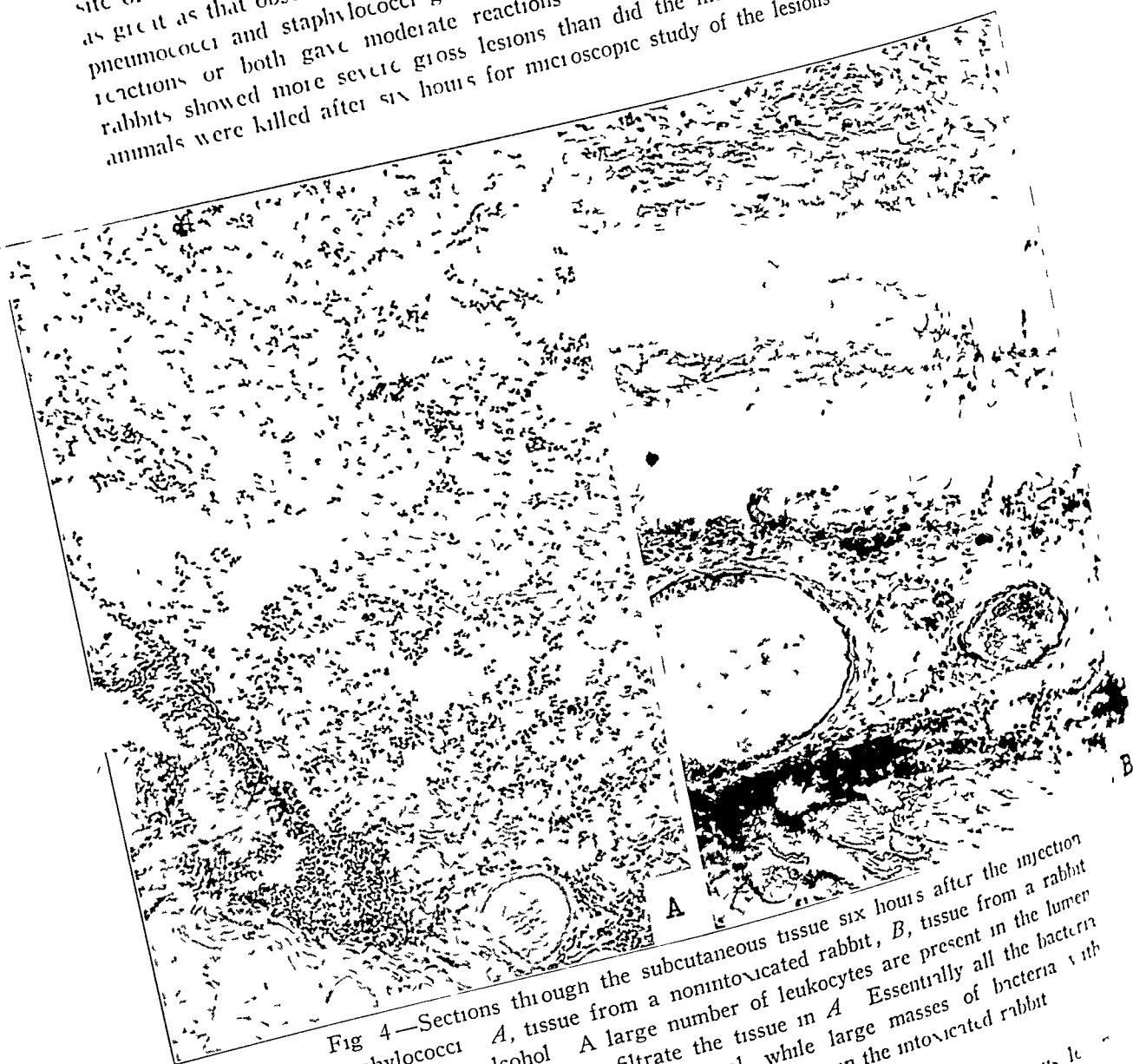


Fig 4—Sections through the subcutaneous tissue six hours after the injection of staphylococci. *A*, tissue from a nonintoxicated rabbit, *B*, tissue from a rabbit intoxicated with alcohol. A large number of leukocytes are present in the lumen of the vessel and diffusely infiltrate the tissue in *A*. Essentially all the bacteria are phagocytosed in the normal animal, while large masses of bacteria with essentially no leukocytosis or phagocytosis are seen in the intoxicated rabbit.

In the rabbits intoxicated with alcohol, in two of the five cutaneous lesions due to pneumococci there was a marked decrease in the number of leukocytes about the bacteria, with many of the bacteria not phagocytosed. The remaining three showed essentially the same leukocytic picture as the controls, that is, leukocytes in the tissue, with practically all the bacteria phagocytosed.

Of the six cutaneous lesions due to staphylococci in intoxicated rabbits, 2 showed a marked decrease in the number of leukocytes, many bacteria remaining unphagocytosed (fig 4A). The remaining four lesions demonstrated the presence of many leukocytes with phagocytosis of bacteria similar to that present in the cutaneous lesions of the control rabbits (fig 4B).

In 5 rabbits anesthetized with ether and with xylene applied to the skin, the hyperemia and edema which developed were grossly the same as those observed in the controls. Microscopic section of the xylene-treated skin removed at six hours showed a decreased number of leukocytes in the area treated with xylene as compared with the skin of normal animals.

Two rabbits anesthetized with ether were given injections of aleuronat in the same way as the rabbits treated with alcohol. At the end of six hours the lesions showed the same amount of edema and hyperemia as was seen in the controls. Microscopic study of the sections of skin revealed a diminution in the number of leukocytes about the aleuronat as compared with the normal reaction.

Pentobarbital sodium similarly did not change the gross inflammatory reaction of the skin to xylene in 5 rabbits or to aleuronat in 4 rabbits. Sections of the skin of the xylene-treated areas after six hours showed practically the same number of leukocytes as the controls. This was true also of sections through the lesions produced by aleuronat. The variation in this group was apparently as great as in a group of normal rabbits.

Mice were used in one group of experiments, in which ether was the anesthetic. Twenty-one mice were used, 14 anesthetized mice and 7 controls. The animals were anesthetized in a large jar containing sufficient ether to maintain anesthesia. After they were anesthetized 0.05 cc of a milky saline suspension of washed staphylococci was injected subcutaneously in each flank of the anesthetized and of the control mice. At one hour intervals up to six hours, 2 anesthetized mice and 1 control mouse were killed, the amount of edema and hyperemia at the site of injection being noted and the tissues fixed for microscopic sections. The macroscopic reaction to the bacteria was the same in the anesthetized and in the control mice.

Sections through the sites of inoculation of bacteria showed that the number of leukocytes increased with the increasing interval between the time the bacteria were injected and the time the animals were killed. There was no difference in the number of leukocytes or the degree of phagocytosis in the two groups of mice.

COMMENT

The results of these experiments indicate that the inflammatory response to an irritant, either bacterial or chemical, is different in a normal rabbit and in a rabbit narcotized with alcohol or ether. Edema and hyperemia are either partly or completely inhibited in the anesthetized rabbit as compared with the normal. There is also a marked diminution in the number of leukocytes in the areas of inflammation in the skin in the narcotized rabbits. The number of animals used in the different groups in these experiments was small, however it is obvious that a variation occurred in the narcotized rabbits. Some of the rabbits given alcohol or ether showed a reaction similar to that seen in the normal rabbits. This variation in anesthetized rabbits differs from the results obtained by Pickrell who found that his intoxicated rabbits in

all instances showed essentially no inflammatory changes in the areas of skin inoculated with cultures of pneumococci

The permeability of the capillaries as demonstrated by the localization and concentration of trypan blue in areas of skin treated with xylene is different in a rabbit given either alcohol or ether from that in the normal animal, as is shown by the altered order of localization and concentration of the dye. In the normal animal trypan blue localizes and concentrates first in the area to which xylene has been applied immediately before the dye is given, in contrast to its localization and concentration first in the areas to which xylene was applied fifteen minutes before injection of the dye in the rabbits given either alcohol or ether.

Although there is a definite difference in capillary permeability in the normal and the anesthetized rabbit as shown by the localization and concentration of trypan blue, we cannot completely agree with Pickrell that "in the intoxicated body the capillaries fail to respond to the presence of an inflammatory irritant with dilatation and an increase in their permeability."

Microscopic studies of skin of anesthetized rabbits into which staphylococci or pneumococci were injected showed a diminution in the number of leukocytes in the extravascular tissue and a failure of these cells to concentrate in the lumens of the blood vessels. This variation in the number of leukocytes may be responsible for the marked difference in the number of bacteria which have not been phagocytosed. This absence of phagocytosis may permit a more rapid multiplication and spread of the infection.

A series of papers has recently been published by a group of German workers¹¹ on the macroscopic variation in the early inflammatory reaction following the administration of certain drugs. The variation in the severity of the reactions in the different groups of rabbits was correlated with the respiratory activities of the animals treated with different drugs. The mechanism diminishing the inflammatory response was considered to be one of respiratory depression leading to a decrease in hydrogen ion concentration of the blood, an increase in the tissue and a reduction in the inflammatory response to mustard oil. Observations

11 (a) Lipschitz, W. Studien zur Pharmakologie der Entzündung. I. Arch. f. exper. Path. u. Pharmacol. **151** 267, 1930. (b) Peng, D. II. Die Atmung und Entzündungshemmung am Kaninchen durch Urethan, *ibid.* **151** 270, 1930. (c) Guggenheim, K. III. Pharmakologische Beeinflussung von Entzündungs- und Entzündungshemmung durch Einwirkung auf die Lungenventilation. Schlafmittel Carduiol *ibid.* **151** 279, 1930. (d) Winkler, H. IV. Die Atmungs- und Entzündungshemmung durch Bromid und die Entzündungsnachwirkung des Urethans, *ibid.* **151** 282, 1930. (e) Fröhlich, H. V. Die Veränderung der Blutreaktion und des Kohlenstoffdioxidgehalts des Plasmas von Kaninchen unter dem Einfluss atemungs- und entzündungshemmender Pharmaka, *ibid.* **151** 323, 1930.

on the frequency and depth of respiration in the rabbits used in our experiments failed to reveal a variation which was considered significant. The number of leukocytes in the circulating blood did not parallel increases or decreases in the inflammatory response in the control or in the narcotized rabbits.

It would appear from our studies that a rabbit anesthetized with pentobarbital responds to the application of xylene, aleuronat and bacteria more like the normal animal than does a rabbit given alcohol or ether. This is interesting in view of some of the other differences in action between the barbiturates and ether, among them the observation of Bollman and his associates¹² that a difference in concentration of the blood occurred in dogs anesthetized with ether as compared with those anesthetized with amytal. Knoefel¹³ also has pointed out that the overstimulation of the sympathetic nervous system and the increased output of epinephrine occurring with ether may be prevented by barbiturates. The failure to observe any difference in the number of polymorphonuclear leukocytes in the cutaneous areas of control or etherized mice in which staphylococci were injected subcutaneously suggests that the effects produced by anesthesia on the inflammatory response may vary in different species.

CONCLUSIONS

1 Capillary permeability in areas of inflammation is altered in rabbits narcotized with alcohol or ether, as demonstrated by the localization and concentration of trypan blue.

2 The inflammatory response may be greatly or only slightly diminished in rabbits narcotized with alcohol or ether, as indicated by the amount of hyperemia, edema and leukocytosis in response to chemical and bacterial irritants.

12 Bollman, J. L., Sirrbek, J. L., and Mann, F. C. Blood Concentration Influenced by Ether and Amytal Anesthesia, *Surgery* **4** 881, 1938.

13 Knoefel, P. K. Anesthesia and the Sympathetic Nervous System, *Anesth. & Analg.* **15** 137, 1936.

JOINT CARTILAGE UNDER INFRAPHYSIOLOGIC, ULTRAPHYSIOLOGIC AND EUPHYSIO- LOGIC DEMANDS

ERNST FREUND, M.D.
LOS ANGELES

The importance to osseous structures of functional efficiency is common knowledge. The Hueter-Volkmann pressure theory, Wolff's law of transformation of bone and Roux's principle of the functional stimuli of pressure and tension have been widely recognized, and the idea that osseous tissue apart from the important factor of heredity is in need by the laity. Physicians are accustomed to observe that osseous tissue adapts itself to changes of functional conditions, it increases under augmented function and decreases in regions in which function is diminished, and this process of adaptation is associated with a complete change of its inner architecture—extensive replacement of the old osseous tissue by new tissue more fit for the new purpose. The process of resorption and apposition of bone which is continuously at work to fulfil the daily demands of altered statics is one of the cardinal features in the biologic nature of the skeleton.

Far less common is the knowledge that the cartilaginous tissue also lives and under normal conditions responds to certain functional stimuli which are as important for growth and existence of cartilage as pressure and tension are for bone. The relatively small amount of cartilaginous tissue present in the adult organism has apparently kept down interest in essentially the same questions which for osseous tissue found conclusive answers several decades ago. It is surprising that cartilaginous tissue which plays such an important role in the phylogenetic and ontogenetic development and the catabolic changes of which are of such great influence in adult life, has evoked but little interest from a biologic standpoint. For the existence of cartilaginous tissue genetic factors are of intrinsic importance, and many structural changes not to be explained simply on a mechanical or a dynamic basis find adequate explanation in a consideration of embryonal processes or evolution. Cartilage is a supporting substance which, after it has served its developmental task as predecessor of bone tissue, is present in relatively few regions, where

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it needs for its further existence and development certain functional stimuli that may be considered almost specific

I am mainly concerned in this article with some of the biologic properties of joint cartilage. The behavior of cartilage under ultraphysiologic conditions (increased pressure) and infraphysiologic conditions (disuse) will be discussed especially. From such an analysis it will appear that joint cartilage reveals its normal highly differentiated (functional) structure as long as the biologic stimuli exercised on it range within physiologic limits. There will be alteration of structure yielding quickly to lasting damage as soon as the duration of the stimuli exceeds the normal. Joint cartilage, like every other highly differentiated tissue, has been rendered almost unable to compensate for pronounced catabolic changes by its lack of power of regeneration which is only a result of the extreme degree of adaptation of this tissue to function. In order to understand this characteristic of joint cartilage it is necessary to be well informed about the normal structure of cartilaginous tissue.

Dependent largely on function, the architecture of articular cartilage varies considerably from joint to joint. There is a different picture in a weight-bearing joint of the lower extremity, where a great deal of pressure is exercised on the joint ends, from that in a smaller joint of the arm (a finger joint for instance), where pressure is relatively mild. The smaller joints, less complicated in their function, show less differentiation in their cartilaginous structure. Age is another important factor. In infancy and youth the structure of joint cartilage, even in the larger articulations of the lower extremities, is less mature. It reaches its full development as a mechanical-functional structure when skeletal growth stops and not before, provided the joint has been used normally.

This means that the high degree of functional differentiation of joint cartilage is gradually attained during postnatal life, in other words, it is exclusively the use of the joint which brings about the mature architecture of the adult joint cartilage. Without normal function, joint cartilage either disappears entirely or fails to acquire functional structure. It may survive and even proliferate, but such survival and proliferation occur only according to its inherent properties of growth and not according to functional or static demands. The structure will be irregular and without the striking economy displayed by tissues under the influence of function.

Joint cartilage can in a general way be considered that portion of the cartilaginous epiphysis which escapes ossification. It covers the bony epiphysis along a surface which even in adult life shows most of the histologic characteristics of the process of enchondral ossification. There is a layer of calcified joint cartilage corresponding to the zone of provisional calcification and there is a subchondral bony lamina which takes

the place of the primary spongy bone as soon as the active process of enchondral ossification comes to a standstill. Although the enchondral ossification along the lower surface of the joint cartilage is of little intensity when compared with the ossification along the diaphysial side of the epiphysial plate, it is nevertheless, as I shall show later, of considerable importance for the definite shape of the bony epiphysis.

What is commonly called joint cartilage is only its noncalcified portion. It is by far thicker than the calcified layer and is especially thick in children because the bony epiphysis has not yet enlarged fully at the expense of the proliferating cartilaginous cap. Here, within the noncalcified layers, the gradual development of a static structure can be observed. In infancy the distribution of the cartilaginous cells is irregular. The cells are small, spindle shaped and arranged crisscross in the soft hyaline ground substance, the water content of which is high. This inherited structure, which still resembles the cartilage of embryonal extremities, is gradually replaced under higher differentiation of the cells and consolidation of the hyaline ground substance.

A mature weight-bearing joint permits distinction of three zones in its noncalcified cartilage, the morphologic manifestations of adaptation to its intrinsic function. The more superficial cartilaginous layers show small flat single cells distributed parallel to the joint surface, often looking like fibrocytes. The collagenous fibers which make up a considerable part of cartilaginous tissue also run horizontally in this zone. They are hidden in an eosinophilic hyaline ground substance, and they can be made visible only by certain preparations. This superficial layer, which is relatively thin, is the gliding layer (Erdheim), or the tangential zone (Benninghoff). Below it is the middle zone, or the layer of passage, with rather irregular distribution of somewhat larger, spherical cartilaginous cells, which may form smaller cell groups and which lie within a slightly basophilic hyaline ground substance. The main part of the noncalcified joint cartilage is formed by the pressure layer (Erdheim), or the radial zone (Benninghoff). This zone shows elongated cartilage cells grouped together in radial direction and surrounded by a strongly basophilic hyaline ground substance. The cells and cell groups become larger and more nearly spherical the closer they are situated to the calcified layer of joint cartilage. This is in part an expression of the functional structure (pressure) of the pressure layer (Erdheim), or part, however, it is a reminiscence of a zone in which proliferation of cartilage occurred during the active stages of enchondral ossification. The collagenous fibers within this zone run perpendicular to the calcified layers, where they are firmly anchored. On reaching the superficial layers they make a sharp turn and run parallel to the joint surface until they reach the margin of the joint, where they again merge with the

deepest calcified layers It is clear that by this firm fixation of the collagenous fibers within the calcified and the elastic noncalcified hyaline ground substance the joint cartilage is well fitted to receive pressure The expressions "gliding layer" and "pressure layer" themselves suggest that gliding and pressing motions influence the structure of joint cartilage

I do not intend to give here a detailed review of the literature concerning the structural adaptation of joint cartilage to function I wish only to mention Benninghoff's conclusive analysis, which revealed the importance of shearing stresses as true functional stimuli of joint cartilage Experimental work on animals to study the influence of lasting pressure on joint cartilage has been done by W Muller and by Koch An excellent histologic study of human material has been made by Scaglietti

The cartilaginous changes resulting from disuse are generally better known than are those resulting from pressure The fact that joint cartilage prospers best if it is treated badly (Fick) suggests that long-lasting periods of rest and exclusion of functional stimuli must lead to alteration of the structure of cartilage This observation can be made over and over again Joint cartilage disappears over areas which have lost contact with their antagonist, it remains preserved over the surfaces in contact Deformed joints, with limitation of motion, changes in the joint axis and in the configuration of the joint ends, dislocated joints and joint ends following exarticulations—all these demonstrate that joint cartilage degenerates and is replaced by fibrous tissue if it lacks contact with its antagonist Immobilization alone which permits good contact of the articular surfaces with each other, i e, persistence of some pressure has proved in many observations not to be greatly damaging to joint cartilage (Reyher, Moll and W Muller) The peril of immobilization does not threaten so much the joint cartilage as the soft tissues around the joint, especially the joint capsule, shrinkage and adhesions of which may result in stiffness of the joint

From all these observations it follows that joint cartilage is in constant need of the stimulus of function for the acquisition of a mature structure as well as for its preservation Unphysiologic demands, i e, overuse and disuse, are met by degeneration and resorption of joint cartilage and replacement by fibrous tissue Most of the data (except those of Scaglietti and Rosi) collected from the literature concern cases in which the joint cartilage suffered from disuse or overuse at a time when it had already reached structural maturity or in which great attention was not paid to this question I give here the analysis of a case in which both factors, disuse and overuse, were working on joints almost continuously for eighteen years after birth It will be of special interest

to study the influence of alteration of function not only on the cartilaginous cover but also on the shape of the growing joint ends

REPORT OF A CASE

The patient was a youth aged 18, with spastic quadriplegia and athetosis. The condition had been present since birth. The delivery had been difficult, but it was not known whether forceps had been used. The patient had never talked or walked. He was able to sit in a wheel chair and to feed himself. He had convulsions frequently, with stridor and severe cyanosis. He had no sense of balance, his head dropped forward. There was athetotic motion of the fingers and wrists. The lower extremities were kept adducted most of the time, with flexion contractures of the hips and knees. There was calcaneovalgus of both feet. Occasionally the patient straightened his knees somewhat, which motion was always accompanied by increased calcaneus position of the feet. Incontinence of all the muscles, more noticeable in the upper half of the body. Incontinence of the bladder and the bowel was also noted. The reflexes were pathologically increased. The patient died of cachexia. Autopsy revealed chronic pulmonary tuberculosis, old tuberculous peritonitis with adhesions between the abdominal organs, tuberculosis of the biliary ducts, hemosiderosis of the spleen and brown atrophy of the liver. The brain at gross inspection appeared normal. General severe cachexia was observed.

When the knee and ankle joints were examined anatomically, a considerable range of passive motion was present. Both sides of the body showed essentially the same changes, therefore, description will be given for one side only. The joints were removed unopened from the cadaver. Formaldehyde was injected into the vessels and the capsule was opened after fixation. The exact topographic relation was thus maintained.

Knee Joint.—The lower end of the femur was shaped unevenly, its transverse diameter was relatively much longer than its anteroposterior diameter. The most striking observation was extensive erosion of the joint surface around the intercondyloid notch, involving mainly the cartilaginous cover of both condyles. The defect of the medial condyle was sharply outlined, the margins of the joint cartilage appeared as though punched out. The denuded area was covered by fairly dense connective tissue, through which the underlying hyperemic bone was shining with bluish stain. The defect of the lateral condyle seemed to be denuded entirely, and the cartilage margin looked as though it had been produced artificially. The joint cartilage surrounding the defect was thin, and because of its thinness the hyperemic subchondral bone made it appear blue. The facies patellaris femoris was in firm contact with the patella, and both cartilaginous contact surfaces were free from erosion. However, where the joint surface of the femur was not covered by the patella, there immediately began the great defect that enlarged into the intercondyloid notch. The superior border of the patella likewise recalled absorption and retraction of the joint cartilages, again in an area which was of contact with the joint surface of the femur. It thus became clear that the huge area of erosion of cartilage was caused primarily by lack of contact of the joint ends. It represented a form of atrophy from disuse.

The medial semilunar cartilage was much smaller than the lateral, and was free from pathologic change. After removal of the semilunar cartilages, it was found that both condyles of the tibia were of even size and the medial condyle was not, as is normal, larger. The portions of the joint surface that were

covered by the menisci revealed a thin joint cartilage of bluish transparency, whereas the central area, which was in contact with the joint cartilage of the femur, showed a thicker, white and opaque cover. These two different portions were separated by a cartilaginous crest, especially on the inner condyle. Such a separation is absent in a normal joint. Both intercondylar tubercles, lying opposite the extensive eroded area of the femur, also showed thinned-out joint cartilage of bluish transparency.

Ankle Joint—The right foot was kept in an extreme calcaneus position, which was a little less marked on the left than on the right. The lower joint surface of the tibia showed a number of changes, most of which were due to retraction of the joint cartilage from the margins. Between the articulating surface of the

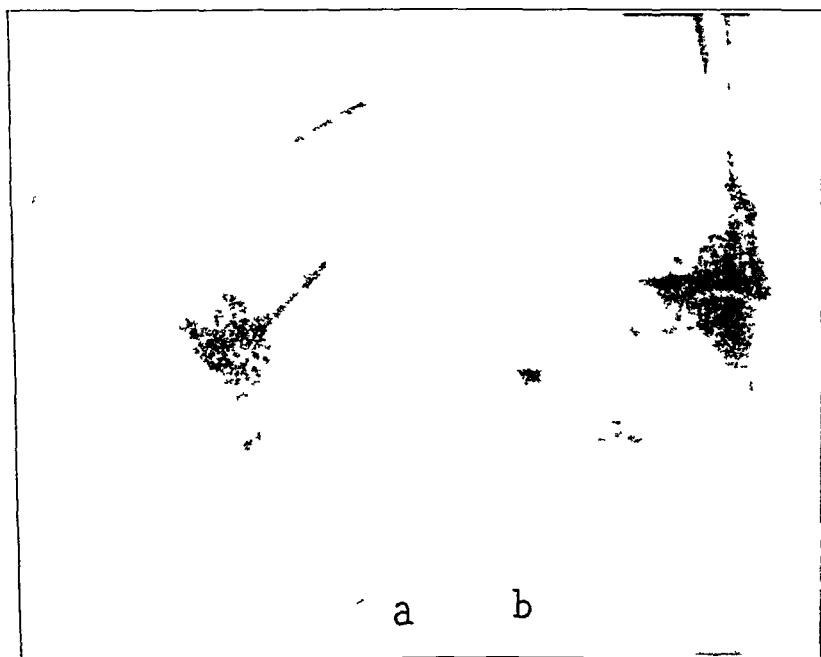


Fig 1—Joints of an 18 year old idiot with spastic articular contractures. *A*, lateral view of the knee joint with flexion contracture and slight posterior subluxation of the tibia. Note the reinforced bony trabeculae in the upper end of the tibia, below the contact surface. The epiphyseal plates are in beginning occlusion. *B*, lateral view of the ankle region. Note the marked calcaneus position with lines of stress going from the lower end of the tibia through the posterior portion of the astragalus into the tuber ossis calcis. Pressure atrophy of the posterior portion of the body of the astragalus and elongation of the neck may be noted.

thinner malleolus and the outer part of the joint surface there was a large area in which the joint cartilage was entirely absent. Similar smaller areas were also present at the anterior margin of the joint, but in this region they did not involve the entire thickness of the cartilage. The lateral portion of the joint surface which faced the fibula was covered by a thin connective tissue pannus,

EXPLANATION OF FIGURE 2

Black and white drawings made from histologic sections of a pathologic joint compared with corresponding areas of a normal joint of the same age

A, longitudinal sections through the body of the astragalus. Section 1, from the idiot with spastic paralysis, is compared with the normal control (2). The letter *a* designates the neck of the astragalus, *b*, the anterior portion of the upper joint surface with good joint cartilage of normal thickness, *c*, the posterior joint surface of the subastragaloid joint, *d*, the eroded area of the joint with flattening of the astragalus. The dotted line indicates the loss of osseous epiphysal substance due to the continuous pressure from the side of the posterior joint capsule and the tight tendon of the flexor hallucis longus muscle. Note the difference in the arrangement of bony trabeculae, they are very dense in the subchondral regions of the normal joint, running from the superior joint surface of the subastragaloid joint in the spastic joint.

B, sagittal sections through the posterior margin of the inner condyle of the tibia. There is marked osteoporosis in that from the idiot with spastic contracture of the joint (1), with persistence of the epiphysal plate, and the joint cartilage (*a*) is thinned out from below and retracted from the joint margin.

C, sagittal sections through the facies patellaris femoris. Compare that from the spastic joint (2) with the normal (1). Section 3 is from the outside of the facies patellares. Note the thinning of the joint cartilage where the femur was without contact with the patella (3) and the normal thickness where it was in contact (2). Note the erosion of the joint surface toward the intercondyloid notch (1) with extreme osteoporosis at this area. An epiphysal plate is observed in the section from the spastic joint with dense cancellous bone at its diaphysal side.

D, frontal sections through the medial condyle of the femur, 1 is from the spastic joint, 2, from the normal control. Note the extreme osteoporosis and deformity. The dotted line shows the great defect of the epiphysis around the intercondyloid notch where the joint cartilage has entirely disappeared.

E, sagittal sections through the patella of (1) the idiot with spastic joint contracture and (2) the normal control. There is relatively little difference, owing to the fact that in each case the patella was in constant contact with the femur.

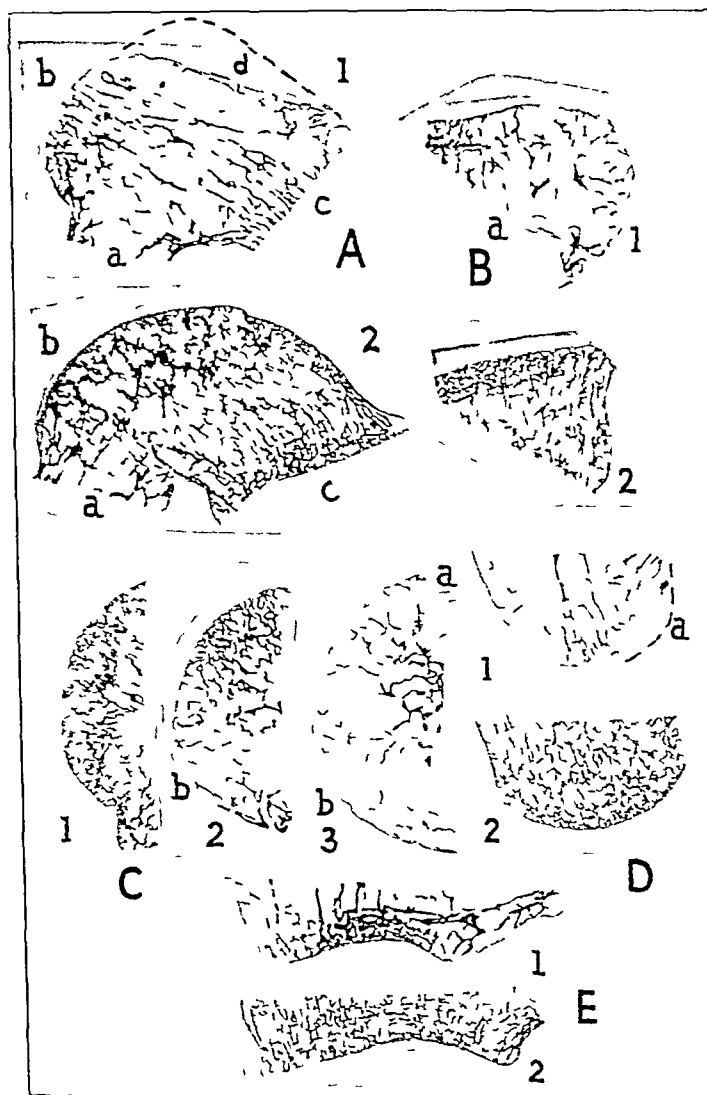


Figure 2

through which the spongy bone showed. The lateral malleolus revealed less marked changes, consisting mainly in retraction of the joint cartilage at the posteroinferior and anterosuperior joint margins.

Astragalus—The astragalus showed the most changes on its superior joint surface. There was an extensive defect in the joint cartilage, involving more than the posterior half of the joint surface. The cancellous bone was so denuded that it seemed as if a whole sector of the upper part of the astragalus had been cut away. It was evident that this alteration of shape had been brought about by maximal dorsiflexion of the foot, which brought the posterior portion of the astragalus out of contact with its joint surface of the tibia and exposed it at the same time to pressure from the side of the overstretched posterior joint capsule and the tendons of the flexor hallucis longus muscle—a paradigm of erosion of cartilage purely by pressure. The anterior portion of the joint surface showed wider extension than is present under normal conditions, and the neck of the astragalus appeared elongated. In this region the joint surface showed another deep erosion into the spongy bone. The defect was covered by fibrous tissue. All the other changes of the astragalus were of minor importance. Corresponding to the defect of the posterior body, both joint surfaces, with the malleoli, were smaller than normal.

Os Calcis—The os calcis showed relatively mild changes of its joint surfaces. Only the posterior portion of the subastragaloid joint revealed more extensive retraction of the joint cartilage where it was entirely out of contact with the astragalus. The anterior part of the subastragaloid joint was well preserved, it seemed even larger than normal.

The right knee joint, the right tibioastragaloid and the subastragaloid joints were examined histologically. Sections from various parts of the joint ends (fifty-one different places) were studied and compared with corresponding sections from the joints of a normal person of the same age.

Summary—The detailed histologic reports may be summarized as follows. The joint cartilage over disused portions rarely reached half the normal thickness. As a rule, it was even much thinner and lacked entirely a functional structure. The whole cartilaginous layer had preserved its embryonal or infantile structure, which means that there was no differentiation into the three typical zones. The cells were not arranged in cell groups. They were spindle shaped or even starlike, densely put together in a hyaline ground substance, which appeared rather soft and even in its deepest layers did not show strong basophilia. Different histologic pictures were observed at the joint margins. The simplest alteration was that of a gradual thinning out of the joint cartilage. It lost its basophilia entirely and resembled dense fibrous tissue rather than cartilage. Finally it disappeared, and the joint surface was represented by a thin bony lamina covered by some fibrous tissue.

A common finding was the following. The structure of the joint cartilage over the disused portions changed considerably. Besides becoming thinned it showed pink-red superficial layers having the appearance more of fibrous tissue of hyaline cartilage. The cells of the deeper layers were much closer together so that at first it appeared as if proliferative changes had taken place. Frequently the dark blue protoplasm showed signs of mucoid degeneration. Finally in the more central layers, which then lost the strong basophilia and appeared silklake. The nuclei also were dark and small, frequently, protoplasmic.

little difference in size between the nuclei in this entirely pathologic area and the nuclei in neighboring areas. The severely degenerated cartilaginous cells were surrounded by halos of ground substance that was much darker blue than is a normal pressure layer. The ground substance, however, was free from signs of degeneration. The distribution of cells in the ground substance was relatively irregular but very dense, so that the proportion of ground substance to cell groups was relatively even. This gave at first view the impression of cellular proliferation, because in a normal pressure layer the proportion of ground substance to cell groups is by far in favor of the former. The actual number of cells and cell groups in this thinned-out cartilaginous portion was as a rule not increased. Only some of the cell groups had enlarged by proliferative activity before they were affected by mucoid degeneration of the cell protoplasm (degenerative hyperplasia).

Most of the cells, however, were simple forms of involution that did not permit differentiation between nucleus and protoplasm. It was clear from these pictures that the marginal portions of the joint cartilage (which under normal conditions are the most active parts and compensate by their proliferation for the daily wear of the superficial cartilage layers) after a short stage of degenerative proliferative activity underwent involution.

This articular cartilage, degenerated by disuse, became resorbed from the joint margin. Different ways of resorption could be observed, the most common being the disappearance of joint cartilage under a fibrous tissue pannus. The pannus could frequently be traced to the synovial fibrous tissue at the margin of the joint, it covered the marginal portion of the joint cartilage for some distance. Typically, the cartilage disappeared incompletely under this pannus, as has been described by Weichselbaum and Pommer. The hyaline ground substance vanished first thus rendering visible the collagenous fibers which it had previously hidden entirely. The fibers resisted resorption and formed a network, in the meshes of which lay the free cartilaginous cells. Wherever a cartilage cell or cell group became opened after removal of ground substance on one side, a sharply lacunar outline in the hyaline ground substance resulted.

As soon as and sometimes even before the cartilaginous cells were freed from the ground substance, cellular proliferation started. Increasing in number, the cartilage cells changed their character and appeared as simple fibrocytes. In many places it was evident that they participated actively in cartilage resorption by enlargement of their own cell capsules and by phagocytic resorption of the surrounding ground substance.

In the first stages this incomplete process of cartilage resorption sometimes presented itself under the picture of Weichselbaum's lacunae. Later the lacunae enlarged and merged, and then there remained a lacunar irregular upper surface of the joint cartilage. With higher power magnification one was always able to demonstrate that the loose network of collagenous fibers immersed into ground substance along the sharp lacunae.

In more advanced stages the joint surface was covered by a loose layer of fibrous tissue which in great part was the product of the incomplete process of cartilage resorption with transformation of cartilaginous tissue into fibrous tissue. This is important because it shows that a fibrous tissue pannus on the joint surface is not necessarily of synovial origin but may be the direct product of incomplete resorption of cartilage.

Gradually the entire degenerated cartilage disappeared, and the primarily loose fibrous tissue became denser, shrunk and finally covered the subchondral bone lamina in the form of a thin but dense fibrous layer.

The osseous subchondral lamella, here and there, was still in connection with small islands of the zone of calcified cartilage, a sure sign that the old osseous lamella was still present. To prevent an opening of the marrow spaces, it had become reinforced, and compared with the other highly porotic bone tissue of the epiphysis it was of considerable thickness. The surface of the denuded bony lamina was sharply lacunar, and the dense fibrous tissue pannus, close to the bone showed loosened texture and resembled a cambium layer. In some areas, where resorption from above was quiescent, several small spots of fibrous osteoid tissue were present under the cambium layer.

It was surprising how sharp, as a rule, was the division line between the used and the disused portions of the joint surface. At gross inspection it was characterized by the sharp, punched-out outline of the retracted joint cartilage. This line of retraction was indicated by the amount of articular excursion in a still movable joint or by the extension of the contact surfaces in a firmly contracted joint. In the latter case, joint cartilage with a rather good functional structure ended rather sharply along a line from which the dense fibrous tissue pannus descended almost at right angles to reach the subchondral bony lamina. Such sharp demarcation best illustrates the dependence of joint cartilage on function. It also shows how circumscribed is the action of the preserving functional factors in joint cartilage.

In areas in which the margin of the joint was covered by vascular fibrous tissue, the origin from synovial fibrous tissue was undoubted. The changes in the joint cartilage were then somewhat modified. Owing to the presence of the synovial pannus, the circulation of nutritive fluids in the joint cartilage was increased far above normal. For this reason the superficial cartilaginous layers appeared slightly swollen by edema of the ground substance and, as a good demonstration of the softening of the joint cartilage, "pseudo-structures" (Schaffer) were present in the form of many sharp lines running parallel to the joint surface. The edema of the cartilage accompanied loss of the basophilia of the ground substance. In these regions were found also the proliferative changes of degenerated deep cell groups, which were the result merely of the greater afflux of nutritive substance through the well vascularized pannus.

COMMENT

It is of interest that exactly the same process of removal of cartilage as was present over areas in disuse occurs in areas where remnants of the embryonal cartilaginous cover of the bony epiphysis become superfluous after the definite joint surface has formed. This process did not represent pathologic disuse of the joint cartilage so much as it did physiologic retraction of joint cartilage from the joint margin. Such parts of the epiphysis as, for instance, the posterior portions of the condyles of the tibia, had never been in contact with the antagonist.

In an early stage the histologic picture of this normal resorption of cartilage consists in formation of small holes by resorption of the ground substance around the deeper cartilaginous cells, a picture which is essentially the same as that in the formation of Weibull's lacunae. The difference consists only in the fact that Weibull's lacunae form in the more superficial layers of joint cartilage.

rule, at a greater age, when they belong to the typical picture of degenerative arthritis. The lacunae in physiologic resorption of cartilage form in the deeper cartilaginous layers and are evidently dependent on nearby

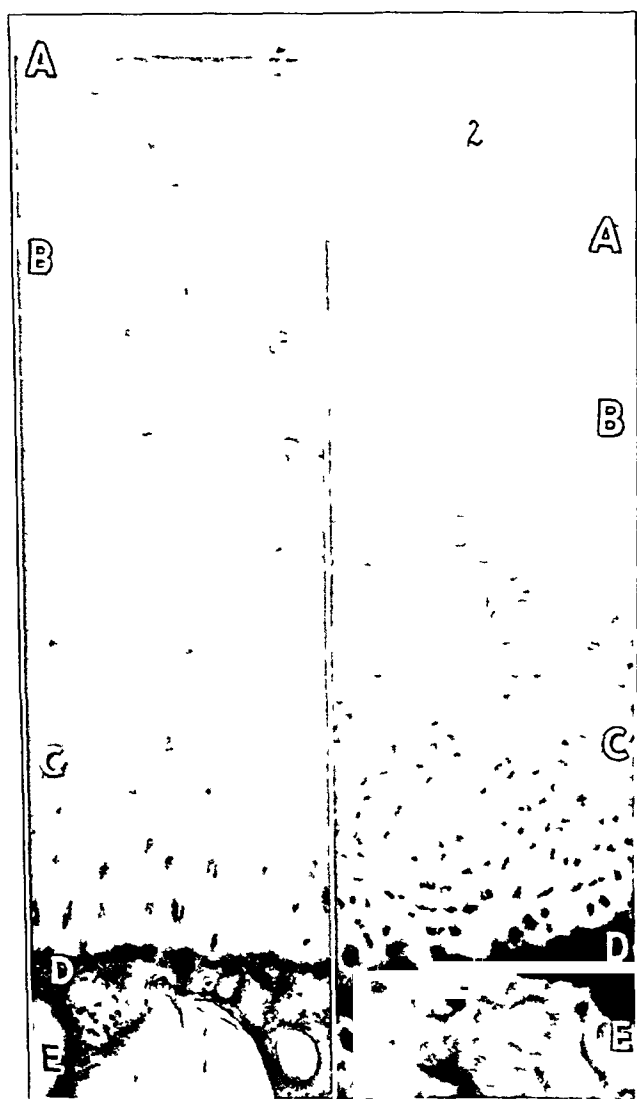


Fig 3—Medial condyle of the femur. The normal condyle (left) is compared with that of the idiot with spastic joint contracture (2) in the same magnification. There is mature functional structure of joint cartilage in the normal joint. *A* indicates the tangential zone. *B* the zone of transmission. *C*, the deep pressure layer. *D* the zone of calcification and subchondral bony lamella. *E* subchondral bone marrow spaces. The differentiation in these different layers is not so distinct in the pathologic joint, the joint cartilage of which is much thinner despite the fact that there is still active enchondral ossification from below.

marrow spaces. The lacunae may enlarge, merge and form greater areas of fibrous tissue lying in hyaline cartilage. The margins of these cartilaginous defects are sharply outlined if the removal of ground substance is incomplete. The cartilage in which such physiologic resorption takes place entirely lacks basophilia even in its deepest layers, and there is no tendency to form large balls of cells as in areas of pathologic disuse. This is the main difference between pathologic and physiologic retraction of cartilage.

Besides the development of these histologic changes in disused joint cartilage, my investigation showed also the influence of infraphysiologic use of the joint surface on the final shape of the joint ends if disuse started early in life. In an adult one can hardly expect great alteration of the bony epiphysis even with extensive loss of joint cartilage by disuse. There may be considerable osteoporosis, but as a whole the subchondral bony lamina will remain preserved. It is different in the case of a growing person. The joint cartilage of a child is relatively and often absolutely much thicker than that of an adult. The bony epiphysis enlarges gradually by enchondral ossification of the joint cartilage. Proliferation of cartilage occurs because of inherited properties and is at least for some time fairly independent of function. Thus it is possible that the contracted joints of a child with spastic paralysis appear normal in the first years of life. Later, however, when function becomes more and more a decisive factor in the development of the joint ends, those portions of the joint cartilage which lack the stimulus of function do not reveal adequate development. The enlargement of the bony epiphysis is not simply represented by resorption and replacement of the deeper layers of joint cartilage, by which process the bony epiphysis enlarges at the expense of cartilage, which becomes thinned out. Enchondral ossification of the cartilaginous epiphysis is also associated with proliferation and proliferation of cartilage are well balanced, so as to leave, when physiologic osseous growth stops a portion of the previous cartilaginous cap of the epiphysis in the form of the articular cartilage.

The importance of function to the cartilaginous structures can be recognized during the first years of postnatal development by the fact that a complex change takes place in the cartilaginous architecture of joints which are under the stimulus of function. Without this the cartilaginous cover remains of the same irregular structure. It does not show any tendency to acquire a mature functional structure. But it also reveals much less proliferative activity of its cells.

One must, therefore, expect that those parts of a growing joint which fall into disuse before the definite normal shape of the joint ends has been reached will remain underdeveloped, because their cartilaginous cover does not keep pace with that of areas which have the stimulus of function. If resorption of cartilage either from above under a fibrous tissue pannus or from below by enchondral ossification is faster than cartilage proliferation, then the entire cartilage cover over the disused portion of the epiphysis will disappear. In a joint which is still growing this loss of cartilaginous tissue is of greater importance than it is in an adult joint. It means that the bony epiphysis which has lost its cartilaginous cover has lost its chance of further increase in size. The joint end will show at this site a defect which cannot be considered a form of simple atrophy from disuse, the condition has followed the lack of enchondral ossification of joint cartilage in the same way as shortening and deformity of an extremity follow premature ossification of an epiphysal plate. The huge defect around the intercondyloid notch in the case which I have described was mainly due to the precocious complete disappearance of joint cartilage over this wide area which was out of contact with the tibia.

This shows clearly that enchondral ossification at the lower surface of the joint cartilage is of great importance for the final shape of the joint ends. Although intrinsic factors, such as heredity, have to be considered first, function, with its definite influence on the growth of the cartilage, is of almost equal value. Physicians have learned to recognize the modeling influence of function on the shape of the long bones. It is known that deranged muscular action may produce osseous deformities. Such deformities develop by direct action on the bony part of the skeleton, the more readily the younger the person (Wolf's law of transformation of bone). My present investigation has shown that deformities in growing persons are not necessarily due to primary disease of the bony epiphyses but are the result of impaired growth of their cartilaginous covering. Early acquired articular contractures, as in my case of the idiot with spastic paralysis, or, even more, congenital deformities in which imbalance of musculature exists, such as congenital club-foot, bring certain areas of the articular cartilages out of contact and to disappearance. The corresponding areas of the bony epiphysis are affected secondarily. They remain underdeveloped because they have no chance to enlarge by enchondral ossification.

However, it is not always the loss of enchondral ossification which accounts for the deformity of the bony epiphysis. Sometimes it is on the contrary hyperactivity of enchondral ossification. In the case described this was evident along the posterior margins of both condyles

of the tibia While in the normal control the joint cartilage extended evenly to the posterior border, in the joint with spastic contracture it was thinner, and the posterior portion of the epiphysis formed a steplike deviation Histologically, the joint cartilage over this area lacked entirely a functional structure It showed the typical picture of joint cartilage in disuse It was clear that the pronounced flexion contracture of the knee joint with the slight posterior subluxation of the tibia had brought the posterior portion of the condyles into disuse Although there was formation of Weichselbaum's lacunae in the superficial cartilage layers, the resorption from above was by no means marked It certainly could not account for the thinning out It rather seemed that the marginal portion of the joint cartilage degenerated under the influence of disuse and, being incapable of cellular proliferation, became slowly thinned out by resorption from below according to the process of enchondral ossification The latter, almost in the same way as it enlarged the bony epiphysis, reduced the thickness of the joint cartilage

The question is why in some places the epiphysis increases in size at the site of inactive joint cartilage while in others it remains smaller The reason lies in the stage of development at which the cartilage is put out of function Around the intercondylar notch, for instance, the cartilage was probably never under the stimulus of function, therefore it disappeared early, leaving the huge defect of the epiphysis The posterior portions of the tibia, however, came out of contact with the femur later, when the posterior subluxation developed which in contracture of the knee joint is a later complication Before this happened, the very portion was in contact with the femur, probably under considerable pressure Released from this pressure, the joint cartilage underwent all the characteristic histologic changes attributable to disuse, but the enchondral ossification from below became more active and led to the steplike bony prominence of the epiphysis From the investigation made by Scaglietti, Rosi and Muller and Joes it is known that pressure on cartilage is a retarding and may even become a hindering factor in enchondral ossification In the case observed by Scaglietti, it is of the joint cartilage but also of the epiphysal plate The animal experiments of Joes and Muller showed the same result except that it revealed also that release from pressure was a new stimulus to growth

At the contact surfaces, the development of the joint cartilage in patient with spastic paralysis compared favorably with that in the person as to thickness and functional structure Especially the cartilage of the patella and facies patellaris femoris was relatively mature, and its thickness over the lateral portion was relatively

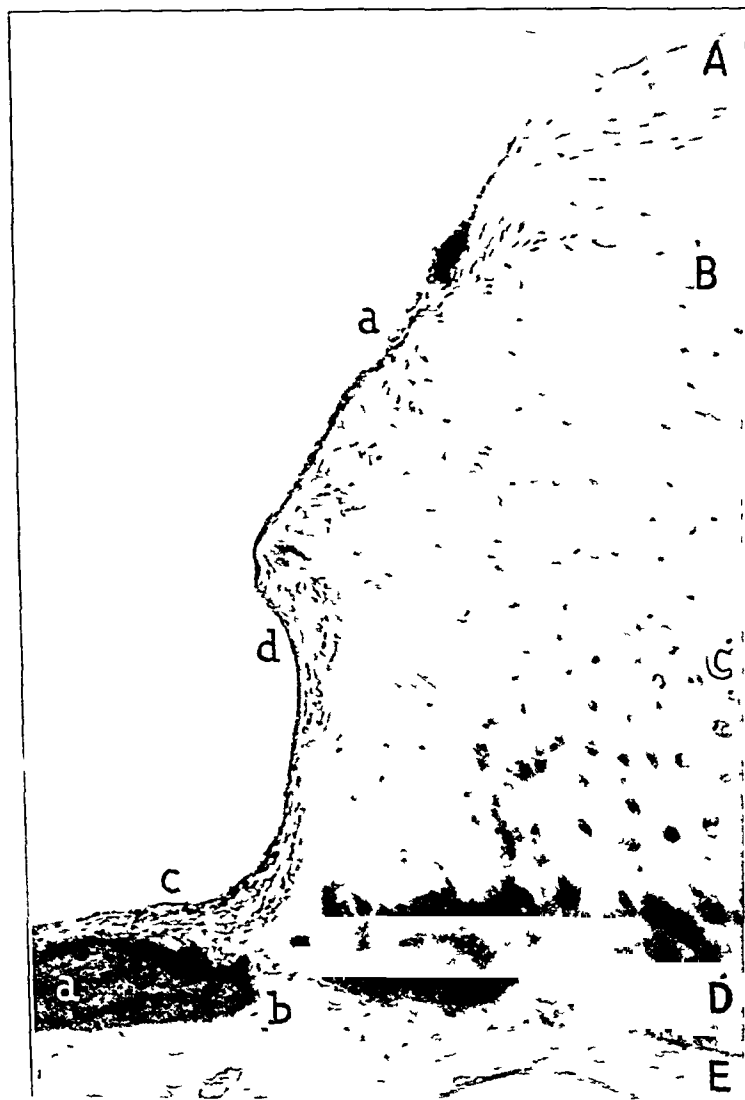


Fig 4—Margin of joint cartilage toward intercondylar notch (faces patellaris femoris) This is the typical picture of "retraction" of joint cartilage. There is good functional structure at the site of contact with the patella. *A* indicates the tangential zone, *B* the zone of transmission, *C* the pressure layer, *D* calcified cartilage with subchondral bony lamina, *E* serous atrophy of subchondral bone marrow. The joint cartilage ends rather sharply along a line where the hyaline ground substance disappears under preservation of the cartilage cells which change to fibrocytes and lie between the exposed collagenous fibers. A fibrous tissue pannus (*d*) results covering the eroded joint cartilage and the exposed subchondral bone (*a*).

than in the normal control. There is no doubt that this extreme development was the result of the continuous pull of the quadriceps muscle on the patella, which pressed it firmly against the lateral condyle of the femur. This pressure effect approximated the physiologic optimum. Degenerative changes were beginning in the joint cartilage of the patella.

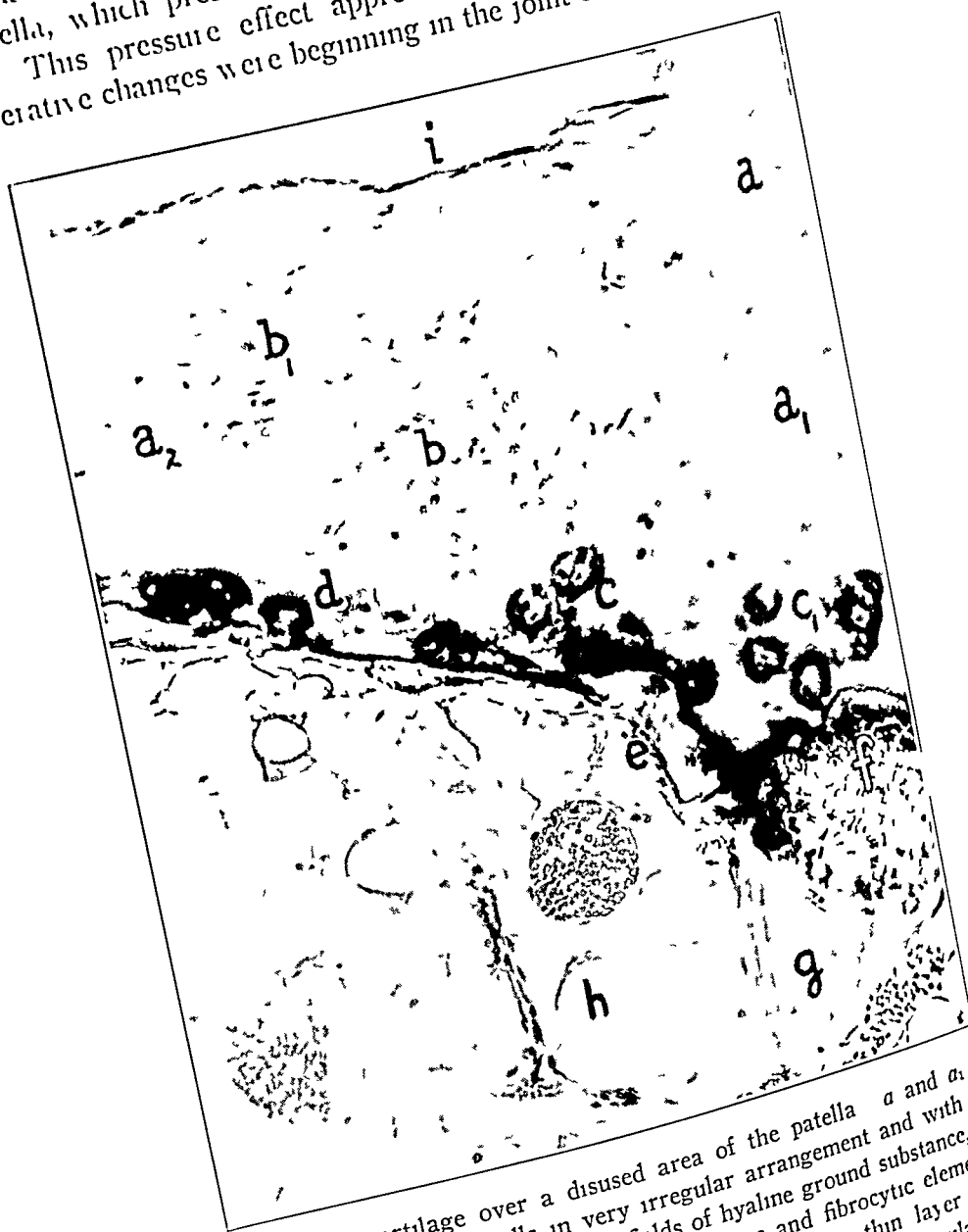


Fig 5—Joint cartilage over a disused area of the patella. *a* and *a*₁ indicate hyaline joint cartilage with cells in very irregular arrangement and with complete loss of normal basophilia, *a*₂, remaining fields of hyaline ground substance, which *b* and *b*₁ disappears, exposing the collagenous fibers and fibrocytic elements. The joint cartilage becomes thinned out and is covered by a thin layer of fibrous tissue, which resembles synovial endothelium. *c* and *c*₁ indicate irregular calcification around the deeper cell groups (*d*), more diffuse in the ground substance, *e*, apposition of bony tissue over the lacunar surface of the calcified cartilage, *f*, vascular resorption, *g*, subchondral spongy bone, *h*, serous atrophy of synovial marrow.

with fibrillation of the superficial layers. These certainly were due to overuse of the joint cartilage. Although the pressure per se did not reach pathologic intensity—on the contrary, for some time it was most favorable to the development of thickness and functional structure of the joint cartilage—it became a damaging factor because of the long period during which it was acting almost continuously. I shall come back to this point a little later.

The joint cartilage over the head of the astragalus was absolutely thicker than the normal. It is certain that this was not a sign of immaturity, though one is accustomed to find thicker joint cartilages in younger persons. There was fully mature functional structure, despite the fact that some active enchondral ossification was still going on (the 18 year old idiot still had open epiphysial plates). Function must have been responsible for this overdevelopment of joint cartilage in the same way as it explained the almost normal thickness of the patellar cartilage. There was

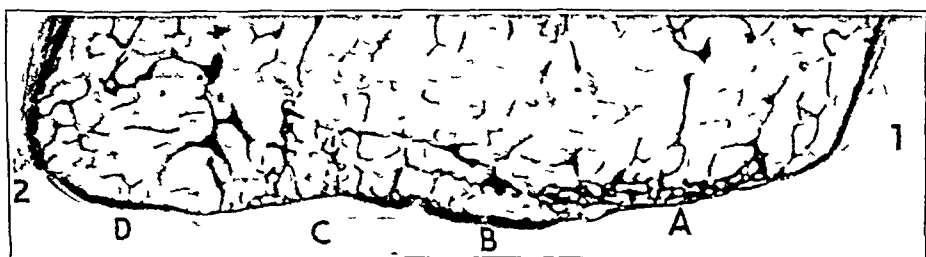


Fig 6—Sagittal section through the medial half of the lower end of the tibia 1, anterior, 2, posterior. A indicates the eroded and somewhat sclerosed anterior margin, B, the compressed portion of the joint cartilage, C, joint cartilage under more physiologic functional stimulus, and D, thinning out of the joint cartilage due to disuse. There is marked osteoporosis of the lower epiphysis.

a striking difference between the poor cartilaginous cover of the tibioastragaloid joint and the almost normal appearance of the subastragaloid joints and the especially thick cartilage in Chopart's joints. If one considers with Roux and Benninghoff the shear or the tangential displacement of the smallest particles within the joint cartilage as the true functional stimulus of the cartilage, then one must recognize that there was a certain spastic motion in these joints which contributed to the good development of the cartilaginous cover. And as a matter of fact, the spastic contracture of the knee joints was released from time to time and the straightening of the knees was associated with increased calcaneovagus position of the feet and with plantar flexion of the toes. Some athetotic motion of the toes was frequent. There can be no doubt that these motions together with the firm contact of the joint ends were responsible for the preservation and even more for the excellent development of the smaller joints of the ankle region.

EXPLANATION OF FIGURE 7

Different portions of the joint surface shown in figure 6 at greater magnifications

A, anterior joint margin with eroded joint surface covered by a thin pannus of fibrous tissue (*b*) which produces some fibrous bone at *b*. At *c* may be seen a small remaining island of old calcified joint cartilage included in relatively dense bony lamina, at *d*, bony trabeculae of rather complex structure with cement and apposition lines, at *e*, advanced serous atrophy of fatty bone marrow. *B*, margin of joint cartilage with pressure damage. Fibrous tissue pannus is seen at *a* extending from the anterior joint margin toward the free joint surface, in communication with the marrow at *b* through a hole in the subchondral hard substance. At *c* loose fibrous tissue is seen, the direct product of transformation of hyaline joint cartilage, which loses basophilia and ground substance at *d*. The deepest layers of the cartilage (*e*) show dense accumulation of dark pyknotic cell groups and irregular junction of the calcified cartilage and the subchondral bone *C*, portion of the joint surface with fairly well developed functional structure of joint cartilage. There is slight depression of the joint level at *a*, due to the lack of supporting subchondral bone. At this area basophilia is absent and the distribution of cells and cell groups is irregular. The bone marrow borders directly on the joint cartilage, owing either to osteoporosis or to still active enchondral ossification. *D*, joint cartilage which under functional stimulus becomes rapidly thinned out toward the posterior joint margin. The superficial cartilage later shows absence of basophilia and cells which resemble fibrocytes, the deeper layers show very dense accumulation of round dark blue cell groups, involution forms a thin pannus of fibrous tissue is present on the surface at *a*. There is extreme osteoporosis, with denudation of the lower surface of the joint cartilage for long distances.

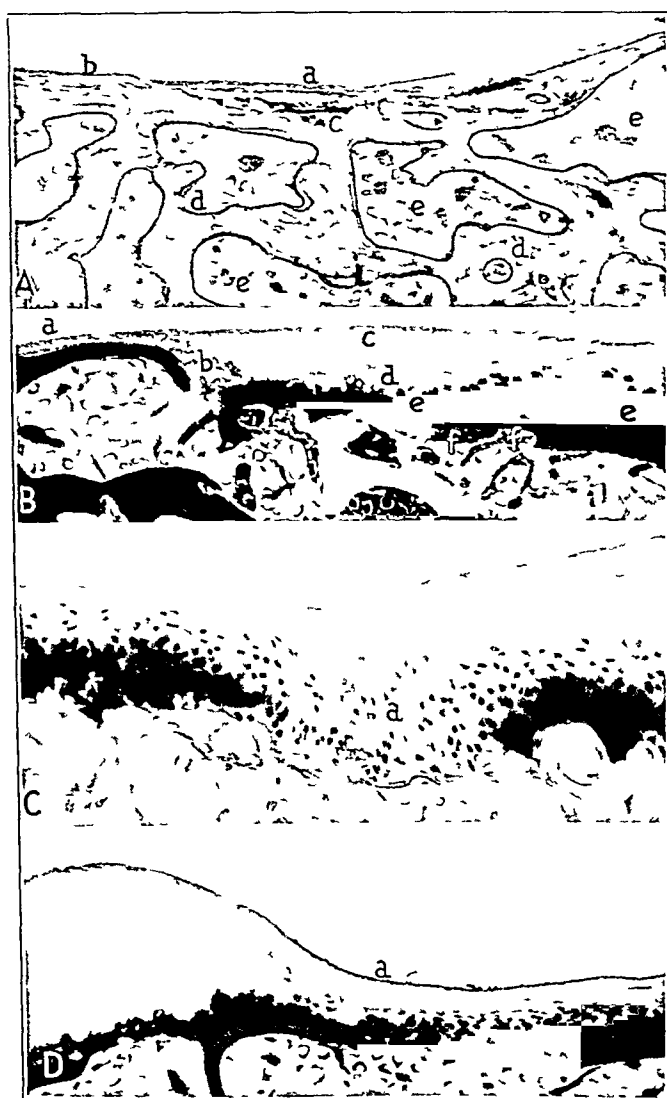


Figure 7

I shall now discuss those articular portions in which joint cartilage meets ultra-physiologic demands. Such places were found in the tibiocalcaneal joint, mainly over the posterior portion of the body of the astragalus but also at the lower surface of the tibia and on both malleoli. Changes due to constant pressure could be studied, from the slightest beginning alteration to the most extensive erosion from cartilage into the subchondral bone. It does not make any appreciable difference histologically whether the damage resulting from compression of joint cartilage was caused by soft tissues, by joint cartilage or by bone. The first changes invariably consisted in a thinning out of the joint cartilage at the point of increased and continuous pressure. This thinning was evidently due to a loss of fluids from the ground substance. It led to complete loss of normal basophilia and to denser arrangement of the cells. With the loss of fluids from the ground substance, the nutrition of the tissue was impaired, and necrosis of cells was common.

The best illustration of pressure damage to a joint was given by the astragalus, the body of which was extremely deformed. It was flattened by the maldevelopment of the posterosuperior joint surface, which presented a large eroded area, a typical pressure sore of joint cartilage and underlying bone. At the posterior margin of the eroded area, joint cartilage was still preserved in a stage which permitted the study of the earlier stages of pressure damage. The joint cartilage was very thin entirely without basophilia and of pink-red stain. It gave the impression of being of slight consistency. In about two thirds of its thickness the cartilage contained, in loose arrangement, cells which resembled fibrocytes rather than cartilaginous cells. The cells showed horizontal orientation, lying parallel to the joint surface, no doubt as the result of compression. Only in the deepest layers were round cells present, these had the appearance of cartilaginous cells. There were absolutely no signs of proliferation.

The severely damaged cartilage underwent disintegration with resorption close to the eroded area. The resorption took place again according to the incomplete process described by Wechselbaum and Pommer. This process reduced the compressed cartilage gradually to smaller islands and caused its worm-eaten appearance. The smaller pieces revealed necrosis of cells, which could also be seen (but to a lesser degree) in the simply compressed joint cartilage which had not yet undergone resorption.

Resorption of the thinned-out cartilage which by compression had become impoverished in substance was mainly from above and under a fibrous tissue pannus which derived from the joint margin. From the bone marrow of the opened marrow spaces or "epiphysal" occurrence of a true pannus, simply by backward development.



Fig 8—Typical picture of changes in joint cartilage, caused by disuse. The lateral portion of the lower joint surface of the tibia is shown. The joint cartilage is thinned out, the superficial layers are bright and the deeper ones dark, owing to dense accumulation of strongly basophilic cell groups. The surface is covered by a fibrous tissue pannus which derives from the joint margin and leads many vessels. There is extreme osteoporosis with serous atrophy of fatty bone marrow.

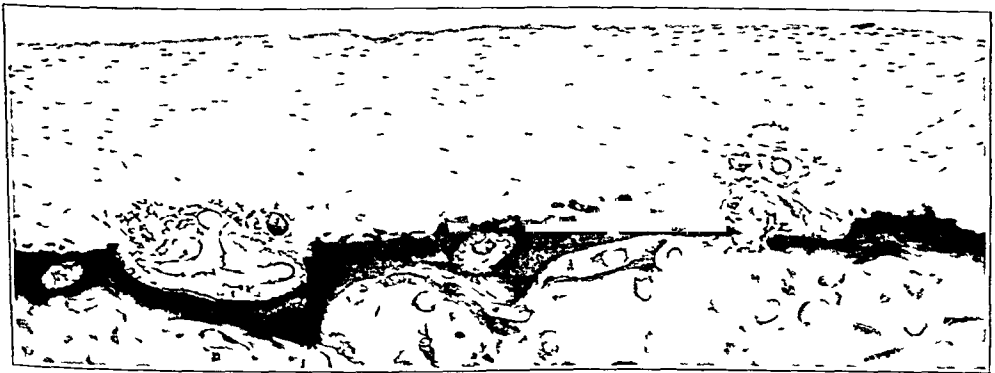


Fig 9—Compressed joint cartilage at the posterior portion of the head of the astragalus. The joint cartilage is thinned out with complete absence of basophilia of the ground substance, even in the deepest layers. The cells are single and very densely distributed, a good many in the deepest layers are necrotic. Note resorption of the joint cartilage from below by bone marrow spaces which contain vessels and which incompletely remove the cartilage. Note also the serous atrophy of bone marrow.

cartilaginous tissue to fibrous tissue, according to the incomplete process of resorption. The further thinning out of the already compressed joint cartilage was then caused by gradual wasting of the most superficial layers, facilitated by washing or pressing out of the hyaline ground substance. Only in a very small portion did cellular resorption of cartilage by chondioclats take place.

Compared with the resorption of cartilage from above, that from below by bone marrow was negligible. Only in a very few places could larger bone marrow spaces be noticed extending into the noncalcified and compressed cartilage. In this region also resorption was incomplete and was sometimes preceded by the formation of Weichselbaum's lacunae. Irregular fibrous spaces resulted, in the margins of which typical blending of collagenous fibers from the degenerated cartilage into young fibrous bone marrow was seen. This was a sign that the

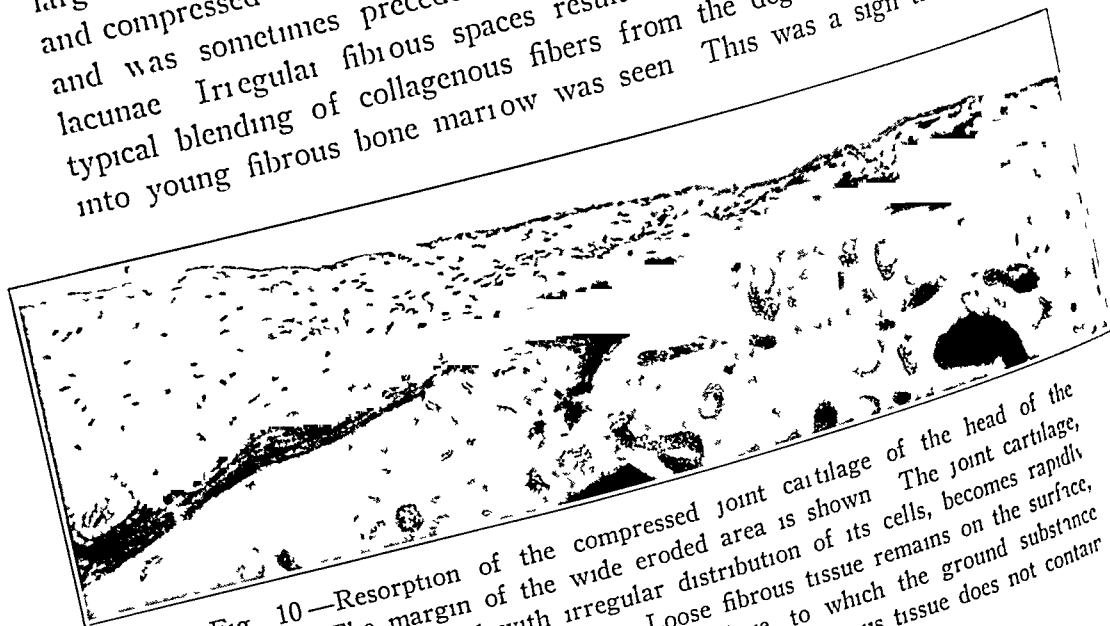


Fig 10—Resorption of the compressed joint cartilage of the head of the astragalus. The margin of the wide eroded area is shown. The joint cartilage, free from basophilia and with irregular distribution of its cells, becomes rapidly thinned out toward the eroded area. Loose fibrous tissue remains on the surface, a product of incomplete resorption of cartilage, to which the ground substance yields but which the collagenous fibers resist. The fibrous tissue does not contain vessels.

degenerated and compressed joint cartilage stimulated the subchondral bone marrow to reactive changes which surpassed occasionally the amount characteristic of simple atrophy. The invasion of noncalcified joint cartilage by marrow spaces is, according to the functional theory of Pommer, a characteristic response to the degeneration of joint cartilage, especially to its loss of elasticity. This is considered by Pommer as pathognomonic of arthritis deformans.

It was of interest to observe that over the area in which there was increased pressure a membrane of fibrinous exudate was present, apparently had connected the joint capsule with the joint surface in sense of beginning fibrous ankylosis. This was also only the consequence of the constant calcaneus position producing constant pressure and traction from the side of the tight joint capsule.

The lateral portion of the astragalus also revealed a most interesting condition. The surface in contact with the lateral malleolus showed posteriorly a definite impression involving the cartilaginous cover as well as the bony epiphysis. The anterior portion of the joint cartilage was of good functional structure. It was smooth and revealed a number of necrotic cells more or less in even distribution, as may be expected at this age in a joint on the way to full functional development. Posteriorly, however, where the astragalus was pressed against the outer malleolus, the structure of the joint cartilage was entirely pathologic. Owing evidently to compression, it was thinned out, which resulted in a flat, troughlike depression of the joint surface. There was a very thin fibrous layer on the surface. This corresponded to synovial endothelium rather than to a fibrous tissue pannus and had but little resorptive activity. The structure of the compressed cartilage differed from the clear functional structure of the neighboring areas. For a short distance, limited to the circumscribed pressure, the cells were dense and were irregularly distributed, while a considerable number were necrotic. The cells in the deepest layers were extremely basophilic and showed pyknosis. The number of necrotic cells became larger as one proceeded toward the center of the compressed area. In the lower two thirds of the cartilage were extensive fields of ground substance which showed only shadows of cartilage cells intermingled with dark blue forms of involution—these resisted the removal of chromatin substance longer. The zone of passage apparently was free from cellular necrosis. The nuclear stain was well preserved, but a number of cells revealed slight mucoid degeneration of their protoplasm. The most superficial layers had very dense arrangement of the cells, which were more fibrocytic than cartilaginous.

From this picture it was clear that the damage to the joint cartilage was due to severe and probably persistent pressure. The deeper cartilaginous layers seemed to be more affected than the superficial ones. The changes were in a relatively early stage, and reactive processes had not yet taken place.

In the more advanced stages, as presented by the large eroded area of the astragalus, the fibrous degeneration of joint cartilage was complete, the cartilage gradually disappeared under the picture of incomplete resorption just as it did over areas in disuse. The underlying bone showed the most extreme degree of osteoporosis, there was only a large cystic area filled with cachectic fatty bone marrow. Despite this extreme atrophy of bone the area of erosion was separated from the marrow by a thin bony lamina which had been displaced considerably toward the center of the epiphysis. This fact alone revealed that the bony lamina was not the old denuded subchondral bony lamina but had been formed during or after the disappearance of cartilage. At the superior surface

of the bony lamina, there was fine lacunar resorption by multinuclear giant cells, and at its endosteal side there was some bone apposition. The combination of both processes brought about the displacement of the bony lamina toward the center of the epiphysis. The bony lamina consisted of mature lamellar bone tissue and was covered by a thin fibrous membrane which permitted recognition of two layers, one superficial, consisting of denser connective tissue with arrangement of its fibers parallel to the joint surface, and the other deeper, vascular, looser and richer in cells. This difference was due only to the difference in mechanical irritation, the deeper layer being more protected. The superficial dense layer may even become necrotic under persistent pressure.

Complete atrophy of joint cartilage through disuse or pressure will lead to deformity of the growing joint ends because of the difference of enchondral ossification. The latter will be retarded or stopped during the period that the joint cartilage is exposed to increased pressure, it is rendered entirely impossible after the joint cartilage has disappeared. If the pressure is marked and persistent, it will lead also to resorption of bone after the joint cartilage has disappeared, and thus the deformity of the bony joint end will increase.

However, the same pressure which is too high for the cartilage may form a stimulus to osseous growth and lead to osteosclerosis rather than to pressure atrophy. This was especially the case at the anterior border of the lower joint surface of the tibia. Here the joint cartilage had disappeared completely, and the subchondral bone was denuded. Osteoid or smaller calcified foci of fibrous bone tissue could be observed over more prominent points of the surface. Under the bony lamina, relatively dense spongiosa was present, with many cement and apposition lines. Small islands of calcified cartilage were included not only in the superficial bony lamina but also in the deeper bony trabeculae. This demonstrated conclusively that the whole system of thick bony trabeculae occupied the site of former joint cartilage which had disappeared under the increased pressure. The exposed osseous tissue, however, had increased in density under the same stimulus of pressure although all the other portions of the tibia showed decided osteoporosis.

In this connection, a few words may be said about the bony joint ends. Extreme osteoporosis was noticed at gross inspection. Corresponding to this but also to the fact that enchondral ossification had not yet ceased the lower surface of the joint cartilage was most irregular. The zone of provisory calcification was interrupted frequently so that bone marrow was bordering immediately at the noncalcified joint cartilage. Closer examination showed that calcification was always present where joint cartilage and bone marrow came together. This indicated the great mechanical importance of the calcification, which in great part

is meant as a fortification of the connection between osseous and cartilaginous tissue. In other words, cartilage calcifies where there is a static or mechanical need for calcification (calcioprotective law of Erdheim). Such cases of extreme osteoporosis, in which the calcium-containing tissues are reduced to a minimum, are excellent examples of the dependence of cartilage calcification on mechanical and static stress which, of course, will be greater where there is connection between cartilaginous and osseous tissue.

The condyles of the femur and tibia showed such a severe lack of osseous tissue that there were wide areas occupied only by bone marrow. The few bony trabeculae were without static arrangement and occasionally showed lacunar outlines. They were of surprisingly complex structure, with many blue cement lines. This was a definite sign that despite the lack of static use and the severe degree of osteoporosis the bone tissue had undergone structural changes. It was not a simple process of bone resorption which gradually reduced the amount of bone tissue but, as always with bone atrophy, a rather complicated process of bone transformation, resorption and apposition changed the entire osseous architecture of the epiphysis. In some areas the few bony trabeculae present were thicker than normal, they often showed perforating vessel canals included in thick inner portions which were crossed by many cement lines (sclerosing osteoporosis).

Those portions of the condyles, however, which were evidently under static stress (they were also covered by joint cartilage of almost normal thickness and good functional structure) revealed considerable density of osseous tissue. The posterior portions were even denser than normal. The relative osteoporosis of these parts in the normal person is easily understood. They are in contact with the tibia only in extreme flexion of the knee joint, a position rarely combined with weight bearing. The constant spastic muscle pull in the contracted knee joint of the idiot brought the posterior portions of the condyles of the femur under ultraphysiologic pressure, which prevented and even overcompensated osteoporosis that in all other places had occurred.

A characteristic picture of atrophy of the fat marrow was associated with the pronounced osteoporosis. The wide marrow spaces, which occupied in some places large cystlike areas, were filled with jelly bone marrow, such as is found frequently in cachectic persons. The reticulum of the bone marrow was easily visible, principally because almost all the capillary vessels were engorged. The fat cells at first view seemed to be decreased in number, and the few which were visible were minute. At closer inspection one found, however, that in many places the cell membranes persisted in their normal dimensions. It was the fatty content of the cells which had shrunk and had frequently even become divided.

into several smaller droplets. The remaining cell area was occupied by a serous fluid apparently rich in proteins. The protein substance appeared as fine eosinophilic granules. The nucleus of the fat cell was found among these granules or, more commonly, at the periphery, as in the signet ring cell. Between the fat cells, especially in areas in which they became smaller after loss of the fat substance, edema fluid was present. Sometimes large free histiocytes of protoplasmic appearance were seen in the edema fluid.

The whole picture was typical of "serous atrophy" of fat tissue as it can best be seen in the bone marrow of cachectic persons. In contrast to the other forms of atrophy of fat tissue, simple atrophy and the *Wucheratrophie* (Flemming), in which the size of the fat cell changes, serous atrophy preserves more or less the normal size of the fat cells, the atrophy concerns mainly the fatty content of the cell, which becomes replaced by serous transudation. In more advanced stages, when shrinkage of the entire cell takes place, halos of edema fluid may be seen around the fat cells, or with complete loss of fat substances the bone marrow may consist only of the remaining reticulum and of edema.

Summarizing, one may say that functional stimuli below or above the physiologic optimum, if active over a long period, are deleterious to joint cartilage. The damage does not remain limited to the joint cartilage in growing persons but draws the bony epiphysis into participation by stopping further enchondral ossification. This point has been entirely neglected by former investigators. They concentrated mainly on the immediate changes in the joint cartilage and attributed more pronounced alterations in the osseous structures simply to atrophy from disuse.

This study of contracted joints revealed also that the time factor is of greatest importance in the development of pathologic changes in the joint cartilages. The pressure force may stay within normal limits, nevertheless, it will damage the joint cartilage if it is active more or less continuously over a long period. The same is true of disuse. Too little or too much use of joint cartilage over a long period is detrimental. This is confirmed by almost every day's operative and autopsy material and does not need proof by animal experimentation. With genu valgum or genu varum, for instance, typically hypertrophic arthritic changes develop in older age. Marginal exostoses and degeneration and fibrillation of joint cartilage will be present at the condyles with increased weight bearing, while atrophy and retraction of joint cartilage are noticed in the condyles with less weight bearing. But even an apparently normal knee joint of an older person will show the dependence of the structure of joint cartilage on function. The joint cartilage of the thin

instance is different where it is covered by the semilunar cartilage and where it is in free contact with the lower end of the femur. In the former region the cartilage is well preserved and smooth (the only significant point is that it is of the yellow color of senile cartilage, whereas young cartilage is bluish white), over the centrum, however, the cartilage is thinned and rough. The explanation is simple. The central portion of the tibial condyles is in constant contact with the condyles of the femur, pressure and friction are here pronounced, whereas the motion between the menisci and the joint cartilage of the tibia is relatively small and permits better preservation of joint cartilage. This difference can be seen even better in genu valgum and genu varum. The central area of the weight-bearing condyle of the tibia may show degenerated, fibrillated joint cartilage, or it may even be denuded and the osseous surface polished and sclerosed, while the marginal portions, covered and protected from too much pressure by the semilunar cartilage, show fairly well preserved joint cartilage.

Whether the pressure force is intense and working over a relatively short period, or whether it is still within physiologic limits but of protracted or even continuous action, the result will be the same. The joint cartilage will lose its normal elasticity and will suffer irreparable damage. Bar found experimentally that the normal elasticity of joint cartilage is impaired considerably by long duration of pressure forces. With the loss of elasticity, the ways are opened for the different processes of cartilage degeneration, even for reactive resorption from below by bone marrow—all changes preceding and accompanying hypertrophic arthritis. One also concludes from this study that there is nothing specific to hypertrophic arthritis or arthritis deformans. Any marked alteration of function for a long period (infraphysiologic and ultra-physiologic demands) is certain to lead to degenerative changes of joint cartilage and may be followed by the whole syndrome of fully developed arthritis deformans, the more probably the longer the joint is exposed to unphysiologic use.

THYROID GLAND A CLINICAL PATHOLOGIC STUDY WITH SPECIAL REFERENCE TO TRUE TUMOR

ANALYSIS OF TWO HUNDRED AND SIXTEEN CASES

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In spite of the voluminous literature and of present knowledge based on extensive experimental studies of certain morbid changes occurring in diseases of the thyroid gland, there still exist, perhaps as in no other field of human pathology, the greatest differences of opinion and the most widespread confusion. Much of the existing divergence and antagonism in views, however, as well as the conflicting interpretations of the thyroid gland both in health and in disease, undoubtedly can be attributed to incomplete knowledge of the structure and physiology of the gland and to its many physiologic and histologic variations and irregularities. This appears to be particularly true as regards the pathologic significance of benign nodules or tumefactions of the thyroid gland and their relation to states of hyperactivity of the gland.

Such tumors or nodules occurring in cases of nodular goiter were for many years considered distinct pathologic entities and were often termed adenomas or fetal adenomas, that is, they were thought to be true benign neoplasms the activity and growth of which were responsible for the anatomic and functional disturbances occurring in patients with symptoms of hyperthyroidism. It is now, I believe, generally agreed as a result of detailed studies that the thyroid gland is an extremely variable organ, particularly influenced by locality and by physical and chemical stimuli and capable of undergoing marked changes in histologic structure resulting from all degrees of hypertrophy and hyperplasia, from the simplest type observed in puberty and in cases of compensatory hypertrophy to the extreme types observed in cases of exophthalmic

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goiter Rienhoff¹ in 1926, from his studies of the involutonal and regressive changes in the thyroid gland following either physiologic or pathologic hypertrophy and hyperplasia, concluded that "these nodules as found in nodular goiter, are nothing more than involutonal bodies, the result of an attempt on the part of the thyroid gland, following a period of hyperactivity to re-approximate its normal histologic structure"

With this in mind, I undertook the task of reviewing and analyzing the results of pathologic examinations of 216 consecutive thyroids surgically removed in cases of hyperthyroidism of varying degree with the purpose not only of presenting a detailed survey of the occurrence of diffuse hyperplasia, nodular goiter and true tumors of the thyroid gland in this series of patients but of properly interpreting and evaluating the pathologic significance of the tumors and their relation to hyperthyroidism. The attempt is based on the extensive studies of Rienhoff and Lewis²

MATERIAL AND METHOD

These specimens consisted of thyroid glands on which partial lobectomies had been performed. They were all fixed in solution of formaldehyde U S P (10 per cent concentration). The series of cases represented by them extended over a period of five years, from October 1930 to October 1935. A few additional cases, although probably authentic instances of these conditions, were excluded, either because the gross material was insufficient or because the reports lacked a suitable histologic description. The gross and microscopic studies were made not on serial sections of the material but on sections of the specimens taken at random, although an attempt had been made to preserve and include all areas of interest for pathologic examination. The gross specimens were inspected with regard to their consistency and translucency and the presence or absence of nodules as seen with the naked eye. The various characteristics of these tumefactions were carefully recorded, that is, whether they were single or multiple, whether they were encapsulated and whether visible colloid or acini were present. When nodules were seen, paraffin sections of the material, stained with hematoxylin and eosin, were reviewed histologically for the purpose of comparative study.

The microscopic examinations took into account the nature of the capsule, the type of nodule, the presence or absence of lymphocytic foci, the follicular epithelium within and without the nodule, the size, shape and contents of the follicles, areas of hyperinvolution or hypoinvolution and the presence or absence of the various sequelae of extreme regression and disintegration, such as fibrosis, hemorrhage, scarring, hyalinization, cyst formation and calcification. In determination of the relation of true benign tumors of the thyroid gland to hyperthyroidism, the clinical histories as well as the pathologic reports and slides were carefully reviewed.

1 Rienhoff, F W. Involutonal or Regressive Changes in the Thyroid Gland, and Their Relation to the Origin of the So-Called Adenomas, *Arch Surg* 13 391 (Sept) 1926

2 Rienhoff, F W, and Lewis, D. Relation of Hyperthyroidism to Benign Tumors of the Thyroid Gland, *Arch Surg* 16 79 (Jan) 1928

ANALYSIS OF DATA

Of the 216 thyroids examined, 139, or 64.3 per cent, showed diffuse hyperplasia and 41, or 19 per cent, nodular goiter. True tumors occurred in 36, or 16.7 per cent. A further subdivision of the third group demonstrated that 25, or 69.4 per cent, were true benign adenomas, 9, or 25 per cent, fetal adenomas, and 2, or 5.6 per cent, carcinomas (table 1). The glands with diffuse hyperplasia were studied chiefly from a statistical point of view, as they presented in practically

TABLE 1—Incidence of Diffuse Hyperplasia, Nodular Goiter and True Tumor in 216 Thyroid Glands

Condition	Number of Specimens	Percentage
	139	64.3
Diffuse hyperplasia	41	19.0
Nodular goiter	36	16.7
True tumor	25	69.4
Benign adenoma	9	25.0
Fetal adenoma	2	5.6
Carcinoma		

TABLE 2—Sex Incidence* of Diffuse Hyperplasia, Nodular Goiter and True Tumors

Condition	Females		Males		Ratio
	Number	Percentage	Number	Percentage	
Diffuse hyperplasia	100	71.9	39	28.1	2.6:1
Nodular goiter	35	85.4	6	14.6	5.8:1
True tumors	25	69.4	11	30.6	2.3:1
Benign adenoma	17	68.0	8	32.0	2.1:1
Fetal adenoma	7	77.8	2	22.2	3.5:1
Carcinoma	1	50.0	1	50.0	1:1

* The total number of thyroids was 216. Of these, 160 (74.1 per cent) were removed from females and 56 (25.9 per cent) from males.

all instances the gross and histologic picture typical of the various types and degrees of hypertrophy and hyperplasia.

AGE AND SEX DISTRIBUTION

Of the entire series of 216 thyroids, 56, or 25.9 per cent, were taken from males and 160, or 74.1 per cent, from females, giving a ratio of 1 to 2.8. Thirty-nine, or 28.1 per cent, of the thyroids removed from males and 100, or 71.9 per cent, of those removed from females showed diffuse hyperplasia, of the thyroids which showed nodular goiter 6 or 14.6 per cent, were from males and 35, or 85.4 per cent, from females, and of the thyroids which showed true tumor 11, or 30.6 per cent, from males and 25, or 69.4 per cent, from females.

From the 36 specimens in the third group, that of true tumors, the following data were obtained. Of the total number of growths, 25 were benign adenomas, 8, or 32 per cent, of these were from males, and 17, or 68 per cent, from females. There were 9 fetal adenomas, of which 2, or 22.2 per cent, were from males and 7, or 77.8 per cent, from females. The 2 carcinomas were equally distributed between the two sexes, of the total number of 216 specimens, the 2 of carcinoma constituted but 0.93 per cent.

A review of the records with regard to age revealed the increasing frequency of diffuse hyperplasia, particularly in women, beginning at puberty and reaching its maximum between the twenty-first and the

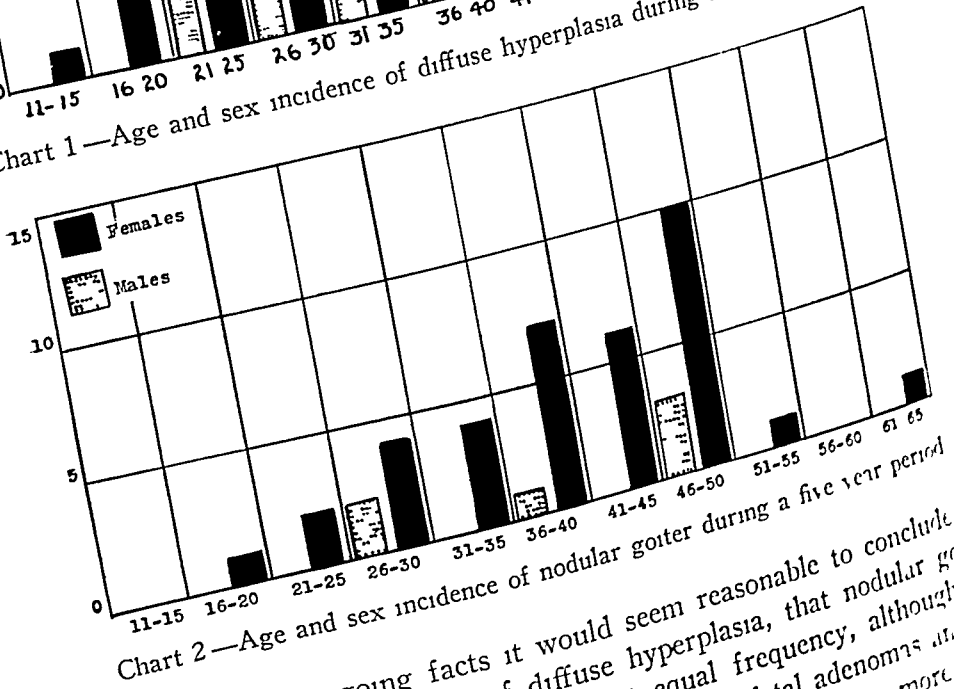
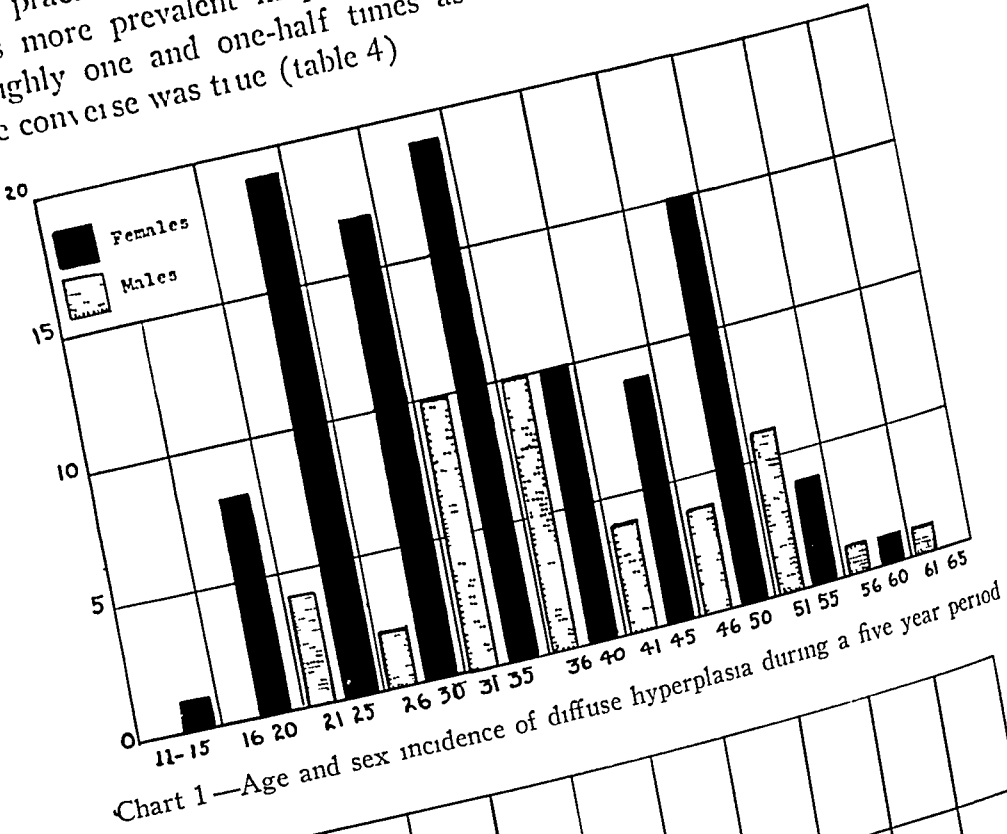
TABLE 3—*Age and Sex Distribution in 216 Cases During a Five Year Period*

Age Years	No of Patients	True Tumors									
		Diffuse Hyperplasia		Nodular Goiter		Benign Adenoma		Fetal Adenoma		Carcinoma	
		Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
11 to 15	2	0	1	0	0	1	0	0	0	0	0
16 to 20	13	0	8	0	1	1	3	0	0	0	0
21 to 25	28	4	19	0	2	0	1	0	1	1	0
26 to 30	32	2	17	2	4	2	4	0	1	0	0
31 to 35	39	10	19	0	4	2	3	1	0	0	0
36 to 40	24	7	7	1	7	0	2	0	0	0	0
41 to 45	19	4	9	0	5	0	1	0	0	0	0
46 to 50	37	4	15	3	10	1	2	1	1	0	0
51 to 55	14	6	4	0	1	1	1	0	1	0	0
56 to 60	6	1	1	0	0	0	0	1	2	0	1
61 to 65	2	1	0	0	1	0	0	0	0	0	0
Total	216	39	100	6	35	8	17	3	6	1	1

thirty-fifth year of life, the period of greatest sexual and ovarian activity (menstruation, pregnancy and lactation).

That the physiologic hormonal influence active during this period may be related to hyperactivity of the thyroid is further evidenced by the sudden rise in the incidence of this condition at the time of the menopause. The incidence in men was constant throughout except for a slight rise during early adult life. Nodular goiter was encountered more frequently with advancing age, especially in women, reaching its peak at middle life and occurring infrequently after that. It was uncommon in persons below 15 years of age. Benign adenomas and fetal adenomas and the 2 carcinomas appeared equally distributed in the two sexes throughout early and late adult life. The younger patient with carcinoma of the thyroid gland was a man 22 years of age. The second carcinoma occurred in a woman 60 years of age (table 3, charts 1 and 2).

A review of the obstetric histories in the 216 cases demonstrated that practically every one of the pathologic states of the thyroid gland was more prevalent in parous than in nulliparous women, occurring roughly one and one-half times as frequently. For benign adenoma the converse was true (table 4)



From the foregoing facts it would seem reasonable to conclude in spite of the preponderance of diffuse hyperplasia, that nodular goiter and true tumors occurred with almost equal frequency, although the benign adenomas by far outnumbered both the fetal adenomas and the carcinomas. Whereas nodules were encountered six times more often in women than in men, true tumors of the thyroid gland occurred twice as often in women.

INCIDENCE OF NODULES

Clerk,³ of Berne, Switzerland, found nodules in more than half the thyroids of the persons over 20 years of age whom he studied and in practically all the thyroids of those past middle life Wegelin⁴ observed tumefactions in 73.3 per cent of the men and in 88.4 per cent of the women past 20 years of age in his series, while Kloppel,⁴ of Freiburg Germany, reported nodose goiters in 81 per cent of persons past middle life Wilson⁶ found diffuse hyperplasia in 79 per cent of his cases and adenomatous nodules in 21 per cent

Jaffe, in the Chicago region,⁷ found nodules in the thyroids of 30 per cent of the males whom he observed and in 44.7 per cent of those of the females Rice,⁸ in Minnesota, examined 493 thyroids, of both

TABLE 4—*Incidence of Diffuse Hyperplasia, Nodular Goiter and True Tumor of the Thyroid Gland in Nulliparous and Parous Women*

	All Thyroids Removed from Females (160)		Thyroids Removed from Parous Women (98 or 60.1%)		Thyroids Removed from Nulliparous Women (62 or 39.9%)		Ratio
	Number	Percentage	Number	Percentage	Number	Percentage	
Diffuse hyperplasia	100	62.5	44	64.0	36	36.0	1.8:1
Nodular goiter	35	21.9	21	60.0	14	40.0	1.5:1
True tumors	25	15.6	13	52.0	12	48.0	1.1:1
Benign adenoma	17	68.0	7	41.2	10	58.8	1.1:4
Fetal adenoma	7	28.0	5	71.4	2	28.6	2.5:1
Carcinoma	1	4.0	1	100.0	0	0.0	

males and females He found that nodules were present in 43.8 per cent of all those removed from males and that the same condition existed in 53.1 per cent of those removed from females

Nolan,⁹ also of Minnesota, in a review of 725 thyroid glands removed intact at autopsy, observed nodules in 191, or 26.3 per cent The 191 thyroids represented a combination of 22 per cent of all

3 Clerk, E Die Schilddrüse im hohen Alter vom 50 Lebensjahr an aus der norddeutschen Ebene und Küstengegend sowie aus Bern, Ztschr f Path **10** 1, 1912.

4 Cited by Nolan⁹

5 Footnote deleted on proof

6 Wilson, L B The Pathology of the Thyroid Gland, Am J M Sc **146**-781, 1913

7 Jaffe, R H Variation in the Weight of the Thyroid Gland and the Frequency of Its Abnormal Enlargement in the Region of Chicago, Arch Path **10** 887 (Dec) 1930

8 Rice, C O The Life Cycle of the Thyroid Gland in Minnesota, West J Surg **39** 925, 1931

9 Nolan, L E Variations in the Size, Weight and Histologic Structure of the Thyroid Gland, Arch Path **25** 1 (Jan) 1938

those removed from males and 42 per cent of all those removed from females

While my statistics on nodular goiter do not show as high an incidence as do those reported by the aforementioned authors, it must be remembered, first, that their material was collected chiefly from the various goitrous regions and, second, that true benign tumors were apparently included in the same category as nodose goiter. All observers agree, however, that a constant increase in the incidence of nodules is seen with advancing age.

STUDY OF NODULES

A pathologic analysis of the 41 specimens of nodular goiter macroscopically revealed that 17, or 40.1 per cent, contained a single nodule and that 24, or 59.9 per cent, had multiple tumefactions. None of the specimens contained more than six nodules. The nodules varied from approximately 0.5 to 5 cm. in diameter. Most of them were firm, yellow or grayish white, localized and encapsulated colloid-bearing areas surrounded by thin or dense gray-white connective tissue. The cut surface was either smooth or granular. A few contained a brown hemorrhagic substance. Others appeared scarred and cystic.

Histologically, the nodular element was composed as follows: Eighteen, or 43.1 per cent, of the nodules presented circumscribed and apparently encapsulated areas consisting of small acini which varied from small round follicles to clusters of three, four and five cells, practically devoid of colloid and peripherally situated. The larger and colloid-containing acini were more centrally located. All of these tumefactions showed evidence of residual hypertrophy and hyperplasia and in many instances hemorrhage, necrosis, scarring, hyalinization and other sequelae of extreme involution existed. In the majority of cases either the fetal or the colloid type of follicle predominated, so that the growths closely resembled mixed fetal and colloid adenomas.

Eleven, or 26.9 per cent, of these tumors were colloid cysts. These appeared as large, scattered, round epithelium-lined structures, varying in size and number and containing an abundance of evenly stained colloid. What was apparently the capsule consisted both of fibrous connective tissue and of compressed normal thyroid follicles. In hypertrophy and hyperplasia and a moderate amount of degenerative change were present.

Five, or 12.9 per cent, of the nodules consisted of thyroid colloid of the fetal type, without colloid and closely resembling so-called fetal adenomas. Four, or 9.8 per cent, were circumscribed areas containing

of numerous large, dilated acini lined with flattened epithelium and filled with colloid. In these the capsule consisted of connective tissue or compressed thyroid parenchyma or both together with evidence of previous hypertrophy and hyperplasia and moderate degenerative changes. Microscopically these tumors were indistinguishable from so-called colloid adenomas.

The remainder of the nodules (3, or 7.3 per cent) consisted of areas made up of small round follicles with tiny lumens and with localized areas of lymphocytic infiltration in the surrounding stroma. Although the epithelium in these areas was hyperplastic, it did not parallel the amount of involutional change noted in the follicular epithelium surrounding them. This fact gave me the impression that these regions had made an abortive attempt to complete the process of involution. Histologically these islands were similar to those described by Ewing¹⁰ and other observers as "miliary or diffuse adenomata." MacCallum¹¹ suggested that "these were areas in which the disease process was beginning all over again." Occasionally, in these tumefactions small mounds of enfolded hyperplastic epithelium were encountered, superimposed on epithelium which had apparently undergone hypertrophy and hyperplasia. This process I termed "adenomatoid hyperplasia," and it appeared to be indicative of secondary hypertrophy and hyperplasia concomitant with a previous exacerbation. In the many instances in which the histologic evidence showed that hypertrophy and hyperplasia had occurred outside as well as inside the nodule, it was some proof that this process had probably been a diffuse one which had involved the gland as a whole instead of being localized and confined to certain specific regions of the organ. Rienhoff, in his study of 109 cases of nodular goiter associated with hyperthyroidism, found this to be true in 34 per cent of cases, the morbid process being localized in 58 per cent. In 1905 MacCallum, in describing the histologic changes associated with hypertrophy and hyperplasia in cases of exophthalmic goiter, stated that this morbid process might be confined "to small patches here and there throughout a gland which otherwise seems normal. Microscopically, the altered areas are quite sharply demarcated from the rest and may involve a great number of alveoli or be limited to very small foci including only a few alveoli here and there."

10 Ewing, J. An Histological Study of the Thyroid, *Tr. A. Am. Physicians* 21: 567, 1906.

11 MacCallum, W. G. The Pathology of Exophthalmic Goiter. *J. A. M. A.* 49: 1158 (Oct. 5) 1907.

It is apparent from the pathologic data on the material so far analyzed that practically every type of involutional irregularity was encountered, ranging from the changes associated with hypoinvolution to degenerative sequelae of extreme regression. This would seem to substantiate the conclusion of Rienhoff, namely, that these tumefactions are not true pathologic entities but are simply the result of the inactive phase of the disease cycle, whether spontaneous or artificial, following a previous overactivity of the thyroid parenchyma. In the pathologic analysis of his cases of nodular goiter, Rice, in 1931, found colloid nodules to be prevalent, occurring in 83.3 per cent of the glands. The parenchymatous nodules, or those resembling so-called fetal adenomas, were present in 25.2 per cent of his cases, and intermediate nodules were present in 8.1 per cent. The latter have the characteristics both of fetal and of colloid adenomas. Degenerative changes were observed in 12.4 per cent of the nodose goiters examined by Rice.

TRUE BENIGN TUMOR

Histologic examination of the specimens considered as representative of true benign tumors showed them to present a fairly characteristic picture of their neoplastic nature. In this group were included 25 simple adenomas and 9 fetal adenomas. Although the latter group showed many of the microscopic features distinctive of fetal adenoma, sections from various portions of the glands containing simple adenomas in some instances presented a heterogeneous picture. While the majority of the circumscribed masses suggested cellular proliferation and regeneration as well, with the typical histologic changes denoting hypertrophy and hyperplasia of the surrounding parenchyma, a few presented evidence of histologic regression, indicating that involution had occurred. In some cases, therefore, it was difficult to draw a sharp line between tumefactions resulting from hyperplasia and involution on the one hand and true tumor growths on the other. MacCallum stated that "the thyroid adenomata are extremely common and here again it is sometimes difficult to feel sure that we are dealing with actual tumors and not with hyperplasia of the functioning gland." Rienhoff, in his series of 109 cases of nodular goiter associated with hyperthyroidism, reported that 8 per cent of the nodules were true benign adenomas.

There is no doubt that the term adenoma as encountered in the literature on the thyroid gland has served as an expression of some of the bizarre histologic interpretations of various investigators. The pathogenesis of this tumor, particularly of fetal adenoma, has also been a point of controversy for many years. Wolfer, cited by Rienhoff,¹² in 1883 introduced the conception of its origin from a terat-

12 Rienhoff, F. W. A New Conception of Some Morbid Changes in the Thyroid Gland, *West J Surg* 39:421, 1931.

rest Wilson, in 1913, characterized "adenomatosis" by diffuse new formation of acini usually involving the entire thyroid gland, beginning with the fetal type without secretion and proceeding to the adult, or colloid, type Goetsch,¹⁴ in 1920 and in 1921, described "diffuse adenomatosis" as the early stage of adenoma and considered the formation of new acini "an abortive attempt at the formation of young small alveoli"

Else,¹⁵ in 1925, in studying the pathogenesis of adenomatosis, which he regarded as a pathologic entity, concluded that the fetal type of acinus arises from masses of undifferentiated cells which are probably identical with those described by Wolfer as interstitial cells. This fetal acinus subsequently develops into a more adult type of colloid follicle. He further stated that "taking the picture as a whole, it gives one the impression of a diffuse new acinous formation in which certain areas have developed more rapidly than others, thus producing the nodular effect"

Hertzler,¹⁶ in 1928, spoke of bosselations and of the development of acini from masses of cells without lumens in the interstitial spaces. Marine and Lenhartz,¹⁷ in 1911, regarded simple and fetal adenomas as benign tumors possessing many attributes of ordinary hyperplasia and some features common to tumors. They explained that "the fetal adenomas have a period of active growth followed by a period of cessation of growth, and finally pass into a colloid or resting state". Fetal adenomas were not affected by iodine, and simple adenomas were only slightly so, in comparison with the ordinary hyperplasias.

Boyd¹⁸ considered nodules of the fetal type as only varieties of colloid adenoma. Murphy and Ahnquist,¹⁹ in 1937, described "fetal pattern," that is, the arrangement of the acinus, and not the acinus itself, as the distinctive feature of fetal adenomas and stated that the appearance of these nodules is really due to the cellular proliferation occurring in a colloid acinus, apparently supporting the growth and thereby eliminating the necessity of fibrous supporting tissue.

13 Footnote deleted on proof

14 Goetsch E. Disorders of the Thyroid Gland. *Endocrinology* 4:387 1920

15 Else J. E. Adenomatosis or the Diffuse Adenomatous Goiter, *J. A. M. A.* 85:1878 (Dec. 12) 1925

16 Hertzler, A. E. Mixed Tumors of the Thyroid Gland. *Arch. Surg.* 16:1187 (June) 1928

17 Marine D. and Lenhartz C. H. The Pathological Anatomy of the Human Thyroid Gland, *Arch. Int. Med.* 7:506 (April) 1911

18 Boyd W. Surgical Pathology, ed. 3 Philadelphia W. B. Saunders Company, 1933

19 Murphy W. B. and Ahnquist G. Origin of Fetal Adenoma in the Thyroid Gland. *Arch. Surg.* 35:211 (Aug.) 1937

RELATION OF TRUE BENIGN ADENOMA TO HYPERTHYROIDISM

In view of the references to "toxic adenoma" constantly appearing in the literature,²⁰ a clinical analysis of the 34 cases of true benign neoplasm was made for the purpose of determining whether the tumors were responsible for the clinical manifestations associated with hyperthyroidism. The clinical records of the patients were consulted, and data on the following points were tabulated for each case:

- 1 Clinical signs and symptoms of hyperthyroidism
- 2 Clinical condition of the thyroid gland
- 3 Preoperative and postoperative basal metabolic rates
- 4 Type of operative procedure
- 5 Preoperative and postoperative diagnosis

Many of the symptoms of hyperthyroidism, such as nervousness, palpitation, loss of weight and tachycardia, were not considered significant in this study, as they are variable factors and are likely to be encountered in conditions other than hyperthyroidism or exophthalmic goiter. Because of this only the objective findings were deemed of any importance.

Clinical analysis revealed glandular enlargement of different degrees in all of these cases. In the majority the mass was symmetric and soft. In a few it was either hard and nodular or soft and nodular. A little more than half of the patients had either visible pulsations of the neck or a systolic bruit at the upper poles. Exophthalmos of varying severity occurred in 15, or 44 per cent, 28, or 82 per cent, had tremors of the lids, tongue or upper extremities. The preoperative basal metabolic rates varied from -10 per cent to $+88$ per cent. The average rate was $+32.6$ per cent. (The patient whose basal metabolic rate was -10 per cent was a boy 15 years of age who had been treated in the clinic for cretinism for the preceding ten years and in

20 (a) Clute, H. M., and Smith, L. W. Cancer of the Thyroid Gland, *Arch Surg* **18** 1 (Jan.) 1929. (b) Williamson, W. G., and Pearse, I. H. The Pathological Classification of Goiter, *J. Path. & Bact.* **28** 361, 1925. (c) Kline, B. S. The Origin of Adenomatous Goiter, *Am. J. Path.* **1** 235, 1925. (d) Marine, D. Special Cytology, New York, Paul B. Hoeber, Inc., 1932. (e) Rienhoff, F. W. The Histological Changes Brought About in Cases of Exophthalmic Goiter, *Bull. Johns Hopkins Hosp.* **37** 285, 1925. (f) Thomas, H. M., Jr. Nodular Goiter with Hyperthyroidism, *Arch. Surg.* **16** 117 (Jan., pt. 1) 1928. (g) Plummer, H. S. The Clinical and Pathological Relationship of Simple and Exophthalmic Goiter, *Am. J. M. Sc.* **146** 790, 1913. (h) Horslev, V. Brown Lecture, *Lancet* **2** 1163, 1886. (i) Biedl, A. Thyroid and Hypophyseal Pathology, *Ann. Clin. Med.* **3** 444, 1924. (j) Halsted, W. S. An Experimental Study of the Thyroid Gland of Dogs, with Especial Consideration of Hypertrophy of the Gland, *Johns Hopkins Hosp. Rep.* **1** 373, 1896.

whom a swelling of the neck had developed during the four years immediately preceding this study. The mass was removed because of its mechanical pressure effect.) The average postoperative basal metabolic rate was $+8.6$ per cent.

The fact that partial lobectomies were performed on all of these patients and were followed in all cases by clinical improvement of the condition and by a fall of the basal metabolic rate would lend some support to the hypothesis that these tumors can become toxic. This, however, is not conclusive proof that the growths and not the concomitant overactivity of the remaining thyroid parenchyma are responsible for the clinical manifestations of hyperthyroidism.

INCIDENCE OF CARCINOMA

In this series of 216 cases primary carcinoma comprised 5.6 per cent of all true tumors, representing an incidence of 0.93 per cent of the total number of thyroids. Clute and Smith,^{20a} in a study of 3,389 cases of disturbance of the thyroid gland, found carcinoma in 67 patients, an incidence of 1.68 per cent. They reported that "an adenomatous goiter preceded the malignant disease in 94.4 per cent of the cases studied." In their group of cases the youngest patient with carcinoma was a woman aged 20 and the oldest a woman aged 82.

Clute and Smith^{20a} stated

Portmann, in Cleveland, reported an incidence of 1.6 percent of malignant disease in persons with thyroid disturbance. Graham found less than 2 percent of malignant disease in thyroids examined at Lakeside Hospital. Eberts and Fitzgerald gave an incidence of 1.8 percent in 612 operative cases of thyroid disease. Craven found carcinoma in 1 to 5 percent of all the thyroids he operated on.

SUMMARY AND CONCLUSIONS

Of the 216 surgically removed thyroids studied, diffuse hyperplasia occurred in 64.3 per cent, while nodular goiter and the true tumors, occurring with almost equal frequency, occurred in 19 per cent and 16.7 per cent respectively.

The frequency of nodular goiter is increased with advancing age, particularly in women.

While there were six times as many women as men with nodular goiter, true tumors of the thyroid gland occurred only twice as often in women.

Practically every one of these pathologic states of the thyroid gland occurred, roughly one and one-half times as frequently in parous as in nulliparous women but for simple benign adenoma the converse was true.

The nodules encountered in most cases of nodular goiter are not true pathologic entities but simply involutional bodies, the result of the involutional cycle of hyperplasia.

Many of these involutional bodies are histologically indistinguishable from true benign adenoma.

While malignant disease of the thyroid gland constituted 5.6 per cent of all the true tumors, the incidence of carcinoma was only 0.93 per cent for the entire group of 216 cases.

There is as yet no conclusive proof that the clinical manifestations of hyperthyroidism are due solely to hyperactivity of so-called true benign adenoma and not to the hypertrophy and hyperplasia occurring simultaneously with the tumor.

ASEPTIC NECROSIS OF THE FEMORAL HEAD FOLLOWING TRAUMATIC DISLOCATION

REPORT OF TWO CASES

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Increasing experience with various histopathologic disturbances of bones and joints has emphasized the frequent occurrence of aseptic necrosis of the head of the femur in fracture and fracture-dislocation at the hip, Legg-Perthes disease, certain congenital dislocations of the hip, and more recently simple traumatic dislocations of the hip. The pathologic process in all of these conditions seems identical, being due apparently to interference with or interruption of the vascular supply through the ligamentum teres. Aseptic necrosis of the femoral head after simple dislocation is attracting special attention because in the majority of cases when the lesion is recognized irreparable damage has already occurred and the function of the hip has been permanently compromised. Yet it would appear that if the potential injury to the femoral head after a dislocation were appreciated and anticipated the treatment might be so ordered that it would prevent much of the damage to the femoral head and would preserve the motion of the hip joint.

A knowledge of the vascular supply of the head and neck of the femur is necessary for an understanding of the pathogenesis and pathologic picture of aseptic necrosis in this region. There used to be considerable difference of opinion in regard to the exact sources of the blood supply to the femoral head. This applied particularly to the part played by the ligamentum teres. It was contended by some that the vessels are patent in infancy and childhood but that all or many of them become obliterated during adolescence and that all are entirely closed during adult life. Recent studies of the blood supply of the ligamentum teres have provided interesting observations. Kolodny,¹ in an investigation of the angiologic structure of the head and neck of the femur, concluded "These results of our study lead us to the conclusion that the blood vessels brought to the head of the femur in the ligamentum teres play a certain role in the nutrition of the femoral head in the new born and children, but are of no perceptible importance in the nutrition of

1 Kolodny, A. The Architecture and the Blood Supply of the Head and Neck of the Femur and Their Importance in the Pathology of Fractures of the Neck. *J. Bone & Joint Surg.* 7: 575-597 (July) 1925.

the femoral head of the adult" On the other hand, Chandler and Kreuscher,² after an anatomic study of 114 round ligaments from 68 adult cadavers varying in age at death from 25 to 75 years, stated "All ligaments contained vessels. In four cases the vessels were of pre-capillary size. All other ligaments contained a significant blood supply." "Serial sections of the junction of the ligament with the femur demonstrate an anastomosis between the vessels in the ligament and those of the head of the femur." Wolcott,³ studying the blood supply of the femoral head, had occasion to examine the round ligaments in 4 old persons on whom reconstruction operations had been performed for ununited fractures at the hip. These patients varied in age from 60 to 75 years. In each case the ligamentum teres had unmistakably patent blood vessels. Zemansky and Lippman,⁴ experimenting on rabbits, concluded that "the vessels of the round ligament are essential, at least in rabbits, for the normal development of the femoral head."

In a study which is currently being conducted in my service at the Hospital for Joint Diseases my associates and I have under observation 5 patients, varying in age between 5 and 15 years, in whom there is unquestionable evidence of the presence of patent arteries and veins in the round ligaments. I have a specimen, a femoral head removed during a Whitman reconstruction operation for ununited fracture of the neck of the femur in a woman 55 years of age, in which a vertical section shows that in the proximal part of the head, over a segment of about $\frac{3}{4}$ inch (1.9 cm.) subjacent and adjacent to the fovea capitis, the bone is reddish (the rest being gray), indicating definitely that the vessels from the ligamentum teres supplied blood to and kept alive this part of the head.

Thus, the head of the femur gets its blood supply from three sources: (1) the interior of the neck, (2) the capsular vessels and (3) the ligamentum teres. The vessels from the ligamentum teres are distributed to a variable segment of the head in the immediate vicinity of the fovea. The capsular vessels supply the periphery and a large part of the head. The blood vessels from the interior of the neck nourish the epiphysal plate. All observers agree that these three sources

2 Chandler, S. B., and Kreuscher, P. H. A Study of the Blood Supply to the Ligamentum Teres and Its Relation to the Circulation of the Head of the Femur, *J. Bone & Joint Surg.* **14**: 835-846 (Oct.) 1932.

3 Wolcott, W. E. Circulation of the Head and Neck of the Femur. Its Relation to Non-Union in Fractures of the Femoral Neck, *J. A. M. A.* **100**: 27-34 (Jan. 7) 1933.

4 Zemansky, A. P., Jr., and Lippman, R. K. The Importance of the Vessels in the Round Ligament to the Head of the Femur During the Period of Growth and Their Possible Relationship to Perthes' Disease, *Surg., Gynec. & Obst.* **49**: 461-469 (April) 1929.

are always present in infancy and childhood. There is doubt in the minds of some whether the vessels in the ligamentum teres remain open in adult life, although there is indubitable evidence from both anatomic and clinical studies that these vessels, at least in some persons, persist even to old age. In most parts of the body there is liberal anastomosis of the vessels entering a given area. This is not true of the femoral head, in which many of the blood vessels are of the terminal type, so that there is poor vascular anastomosis. Interference with or interruption of the blood supply to the top of the head through the ligamentum teres therefore is likely to be followed by aseptic necrosis of the bone and cartilage in the involved area. The extent of the original necrosis in the event of damage to the ligamentum teres is manifestly dependent on the collateral circulation available from the capsular arteries. Chandler⁵ stated "Those areas which are less liberally supplied with vascular anastomoses necessarily have lower factors of safety and become more vulnerable to the effects of vascular interruption." The literature now contains reports of cases in which trauma caused injury to the ligamentum teres with consequent necrosis of the top of the femoral head, the patients including both children and adults. Phemister⁶ reported 4 such cases. Chandler and Kreuscher² reported 1 case of aseptic necrosis of the femoral head following a fracture of the acetabulum and central dislocation of the femoral head. At the last meeting of the American Orthopaedic Association, Potts, of Buffalo, reported 5 cases of aseptic necrosis of the head of the femur, the lesion in each instance following a traumatic dislocation. I wish to record 2 cases in which aseptic necrosis followed traumatic dislocation of the hip, the patients being young adults.

Buchman and I⁷ have found in operating on patients for chronic marked slipping of the femoral capital epiphysis that if after operative realignment and pegging of the head and neck of the femur we prevent direct weight bearing on the femoral head for one year and in some cases even longer (up to two years) the femoral head gradually becomes revascularized and reformed by the process of creeping substitution so well described by Phemister. In the cases of aseptic necrosis of the femoral head following dislocation so far reported there resulted great deformity of the head and disturbance of articular function, even to ankylosis. In every one of these cases, however, weight bearing was

5 Chandler, F. A. Aseptic Necrosis of the Head of the Femur, *Wisconsin M. J.* 35:609 (Aug.) 1936.

6 Phemister, D. B. Fractures of Neck of Femur, Dislocations of the Hip, and Obscure Vascular Disturbances Producing Aseptic Necrosis of Head of Femur, *Surg., Gynec. & Obst.* 59:414-440 (Sept.) 1934.

7 Kleinberg, S., and Buchman, J. The Operative Versus the Manipulative Treatment of Slipped Femoral Epiphysis with a Description of a Curative Operation. *I. A. M. A.* 107:1545-1551 (Nov. 7) 1936.

permitted within an average of three months after the injury, which is, I believe, much too early. In other words, not only was there an interruption of the blood supply to the top of the femoral head, with consequent necrosis of the summit of the head, but weight bearing hastened the collapse of the affected bone.

From a review of the cases of aseptic necrosis of the femoral head following traumatic dislocation reported in the literature and from my own experience, the various aspects of the illness may be summarized in the following manner:

CLINICAL HISTORY AND COURSE OF THE ILLNESS

The original injury is a traumatic dislocation. After the reduction, which in some instances is difficult and may entail considerable forcible manipulation, the roentgenogram shows a satisfactory replacement of the femoral head, which appears normal in structure and outline. There is naturally some pain and disability, and for several weeks the patient remains in bed. As the discomfort subsides, walking is begun, at first with the aid of crutches or a cane and soon without any external support. Walking becomes increasingly easier, and the patient, usually a young adult, becomes active and may even engage in various sports. After several months there reappear some discomfort in the limb and stiffness at the hip. At the beginning these symptoms are present only when the patient begins to walk. There is difficulty in getting into and out of a chair. Soon the patient finds that he cannot run or walk as well, as far or as fast as he used to. The stiffness and pain increase and become constant.

Physical examination reveals a limp. The hip is moderately flexed and adducted, and all motions are restricted to variable degrees. Forced motion, as on manipulation, is painful. There is little or no local tenderness and no shortening.

The roentgen picture shows a lesion in the proximal segment or summit of the femoral head. In the early stages one sees a distinct line of demarcation between the pathologic and the normal bone. This corresponds roughly to the region directly above the epiphysal plate. In the summit of the femoral head the articular surface is irregular and the texture of the bone is altered, it is very dense, with some spots of rarefaction. In the later stages there may be some loose fragments of bone and, not infrequently, osteophytes projecting from the periphery of the head of the femur. This bony hypertrophy is the result of the effort at repair contributed by the capsular vessels. Ultimately there is extensive arthritis, with partial or complete ankylosis.

Gross Pathologic Picture—On exposing the hip joint one finds congestion and thickening of the capsule with hypertrophy of the synovial lining. There may be some loose fragments and spicules of bone.

about the head at its junction with the neck. The top of the femoral head is uneven. The cartilage may be raised from the underlying bone (so-called blistering). Parts of the cartilage may be eroded or entirely loose. There may be cracks in the cartilage. The subchondral bone appears bloodless. If a drill is inserted into the head no blood is obtained until the drill perforates the bone distal to the epiphyseal plate.

Microscopic Pathologic Picture—The synovia is thickened and congested and may show collections of lymphocytes. The subchondral bone shows necrosis but no inflammatory tissue, that is, there is aseptic necrosis with collapse of the bony trabeculae. There is hyaline degeneration of the articular cartilage. The histopathologic picture is much like that of Legg-Perthes disease.

In all of the cases thus far reported, early weight bearing was permitted. It is not possible to state what the ultimate changes would have been had the femoral head not been permitted to bear weight. However, from my experience in the treatment of chronic slipping of the femoral capital epiphysis (I do not permit direct weight bearing for a year or longer) I believe that if after reduction of a traumatic dislocation in a young person weight bearing were prohibited, the collateral circulation from the capsular vessels and the vessels of the femoral neck would in time revascularize the damaged section of the head, which ultimately, through creeping substitution would be replaced by normal bone.

REPORT OF CASES

CASE 1—Thomas C., 16 years old, was admitted to my service at the Hospital for Joint Diseases on March 20, 1938. His chief complaints were pain and stiffness in the right hip. He had fallen from a milk truck on Feb. 11, 1937, sustaining a dislocation of the right hip. The dislocation was reduced, and a plaster of paris spica was applied. This was removed at the end of three weeks, and the patient was allowed to walk, using a cane, which was discarded two weeks later. He rapidly increased his activity and shortly was playing basketball. In October, eight months after the injury, the hip became painful and he began to limp. Soon thereafter it was noted that the affected limb was shorter than the opposite limb.

Examination on admission showed the patient to be in good general condition, walking with a marked limp on the right side. The right lower limb was in an attitude of flexion, adduction and outward rotation at the hip. The angle of greatest extension at the hip was 145 degrees, that of flexion, 110 degrees. There were a few degrees of rotation and no abduction or adduction. There was no local tenderness at the hip but there was 1 inch (3.1 cm.) atrophy of the thigh.

Roentgen Examination—The original roentgenogram (fig. 1 A) dated Feb. 12, 1937, showed a dorsal dislocation of the hip. After the reduction a roentgenogram (fig. 1 B) showed that the femoral head was normal in shape, size and structure. There was no evidence of damage such as fracture, to the head itself. The film (fig. 2) made on March 20, 1938, thirteen months after the injury, showed an extensive lesion of the femoral head. The top of the head, above the epiphyseal line, appeared as a dense crescentic mass with some normal-looking bone at each extremity. Underneath this dense bone was a ragged line of rarefied tissue pre-

sumably the epiphyseal cartilage, below which was a border of sclerotic bone. The neck at the upper extremity of its outer border projected upward beyond the head as a large conical spicule. The acetabulum showed no gross abnormality. The top of the femoral head appeared like a sequestrum.

Operation.—An operation was decided on for the purpose of drilling through the femoral head and neck in the hope of revascularizing the sclerotic head. The hip was exposed through an anterior Smith-Petersen incision. When the capsule was cut through there was a gush of fluid, this proved on culture to be sterile. When the capsule was retracted there came into view three strips of articular cartilage 1 by $\frac{1}{4}$ inch (2.5 by 0.6 cm), attached to one another and to the outer surface of the femoral head but loose and raised from the bone in their centers. The femoral head was enlarged, the fovea could not be identified. On the anterior surface of the neck was a flat osteochondral mass entirely free except at its base, where it was attached to the neck. This was removed. The neck was everywhere covered by synovial tissue, which in places was $\frac{1}{2}$ inch (1.3 cm) thick and



Fig 1—*A*, roentgenogram taken Feb 12, 1937, before reduction, showing the femoral head out of and above the acetabulum. *B*, roentgenogram taken February 13, directly after the reduction. Note the replacement of the femoral head in the acetabulum. There is no evidence of injury to or deformity of any part of the head of the femur.

markedly congested. The inner surface of the capsule was entirely covered with thick, beefy synovial tissue. The head of the femur was then dislocated from the acetabulum. There was no ligamentum teres. Around the upper two fifths of the head was a circular linear depression. Within this area the articular cartilage was rough in some spots, eroded in others and entirely loose in several places. At the line of depression the cartilage was thin, and there were two loose ribs of cartilage, one on the anterior and the other on the posterior surface of the head. Twelve drill holes were made through the disorganized cartilage on the surface of the head. These penetrated the neck. The subchondral bone was abnormally soft in some areas and very hard in others. After each drill hole was made some moments passed before blood appeared. Evidently, the subchondral bone was anemic and the blood welled up from the deeper bone in the femoral neck. The acetabulum on inspection and palpation seemed normal. The femoral head

replaced in the acetabulum, the wound was closed without drainage, and a plaster spica was applied

The gross pathologic observations consisted of (1) an enlarged femoral head, (2) absence of the fovea capitis, (3) absence of the ligamentum teres, (4) a circular depression on the top of the head, including within its confines about two fifths of the head, (5) irregularity and looseness of the articular cartilage, (6) numerous cartilaginous tabs, (7) extensive synovitis and (8) two osteochondral bodies projecting from the femoral neck

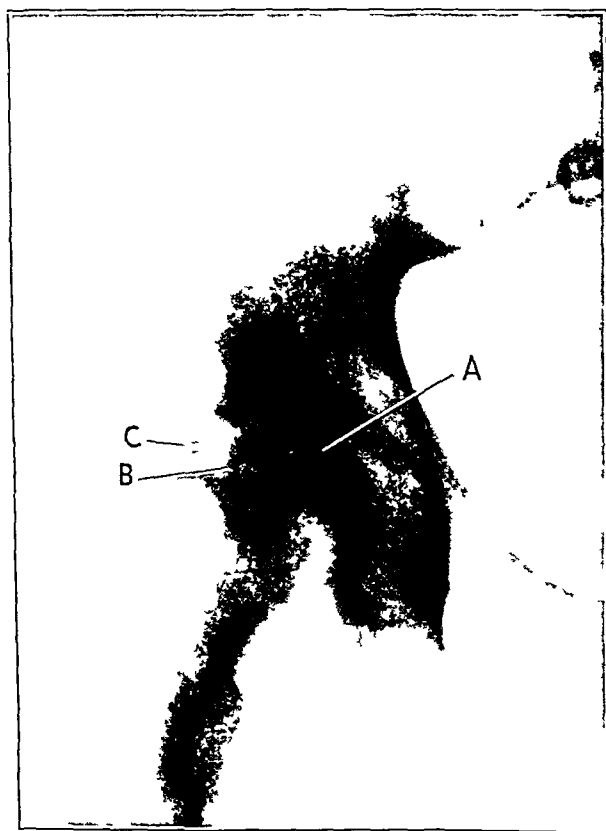


Fig 2—Roentgenogram taken March 20 1938 There is deformity of the femoral head The summit of the head is sclerotic and is the site of aseptic necrosis (A) At B are seen the remains of the epiphyseal plate Note (C) an osteophyte this represents an effort at repair on the part of the capsular blood vessels supplying the periphery of the head

The patient is still under observation walking with a Thomas caliper brace and an ischral crutch and receiving physical therapy for mobilization of the hip joint It is too soon to be certain of the ultimate result of this late operative intervention

The various specimens removed from the hip joint (fig 3) showed (1) villous hypertrophy of the synovial membrane which contained in places collections of lymphocytes (2) degenerated articular cartilage and (3) necrotic bone

Summary of Case—I believe that in this instance the pathologic condition in the hip was a sequel to a tear of the ligamentum teres during the original dislocation. The blood supply to the top of the head was thereby cut off, and the subchondral bone and articular cartilage died from inanition. The top of the head became a loose body. There resulted a reactionary inflammation in the capsule and synovial tissue. The damage to the femoral head from its loss of blood supply was increased by weight bearing, which crushed the bone and accelerated the degeneration of the tissue before an adequate collateral blood supply could be established.

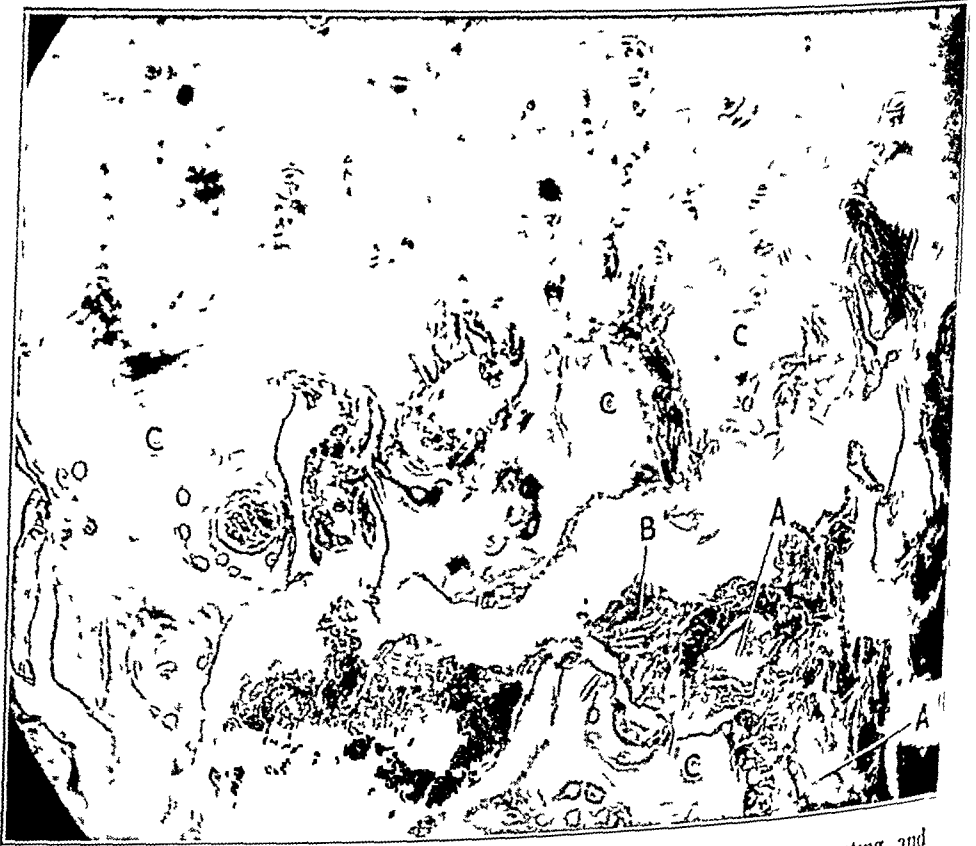


Fig 3—Photomicrograph showing necrosis of bone (A) fragmenting and necrosing bone, (B) detritus, and (C) dead bone

CASE 2—Herbert S., 20 years old, consulted me on June 3, 1938 for stiffness in the right hip and pain in the right knee. He had dislocated his right hip in September 1937 in an automobile accident. The dislocation was reduced with the patient under the influence of an anesthetic, and a plaster of paris support was applied. This was removed after four weeks, and physical therapy was instituted. He improved at first very rapidly, during February and March he had free motion in the hip and was engaging vigorously in athletics. Since then pain and stiffness have set in, so that at the time of writing he has less motion in the hip than in March. In particular, he has difficulty in getting into and out of a chair.

Examination showed him to be in excellent general condition. He walked with a limp on the right side. Extension of the hip was normal, while flexion was checked at 80 degrees. Abduction was limited to 5 degrees and adduction to 10 degrees.

degrees. Rotation was restricted to a fourth of the normal range. The limbs were of equal length.

Roentgen Examination—A roentgenogram made in October 1937, several weeks after the dislocation was reduced, showed not only that the head of the femur was in the acetabulum but that the head appeared normal in contour and structure. There was a shadow, as of a sliver of bone lying along the lateral margin of the head and neck, extending down to about $\frac{1}{2}$ inch (1.2 cm.) of the greater trochanter. There was no defect anywhere to indicate the origin of this fragment of bone. A roentgenogram made on November 26 showed that the articular cartilage of the femoral head was smooth. The para-articular shadow had almost completely disappeared. A lateral view showed a little rarefaction and an oblique indentation in the outer surface of the head at its junction with the neck. Roentgenograms made in April 1938 exhibited a marked alteration in the architecture of the femoral head. There was sclerosis of the top of the head with irregular rarefaction at the epiphysal line. The joint was hazy. One film showed a line of rarefaction extending from the articular surface, a little to the inner side of the fovea, obliquely downward and outward to the junction of the head and neck. There was a bony spicule formation at the junction of the head and neck on the outer side, at the extremity of the oblique line of rarefaction or depression. The previously noted para-articular shadow was represented by two small pieces of bone. The articular cartilage of the head was hazy and irregular. There was rarefaction of the juxta-epiphysal bone in the neck. Roentgenograms made on May 19, eight months after the injury, showed irregularity of the articular cartilage of the femoral head, rarefaction of the neck of the femur, some loose fragments of bone and marked sclerosis of the upper segment of the head.

Summary of Case—In this, as in the previous case, not only was the circulation of the head disturbed by a tear of the ligamentum teres during the dislocation, but the resumption of weight bearing four weeks later further traumatized the femoral head, causing disorganization of its upper segment. The final result was necrosis of the top of the head and severe disturbance of the function of the hip joint. There was one factor in this case which was not present in case 1, namely, the presence of a shadow of ossific density in the lateral portion of the hip. Whether this represented calcification and ossification of a portion of the capsule that was injured or an actual fracture of a part of the head cannot be decided except by opening the joint. Otherwise the history, course and roentgen changes are similar to those noted in the first case.

TREATMENT

The treatment given my patients after the reduction of the dislocation may have appeared logical in that function was resumed when the irritative symptoms following the injury subsided, but in the light of the ultimate poor function it was not satisfactory. I have indicated why early weight bearing has a harmful effect. The ability of the patient to resume walking within a few weeks after so severe an injury as a traumatic dislocation of the hip may be gratifying to the surgeon and the parents but with an eye to the ultimate service of the hip it is imperative that weight bearing be interdicted until it is safe. While I have no cases of aseptic necrosis of the femoral head to prove the truth of my suggestion I may refer to the value of walking without weight bearing

in cases of Legg-Perthes disease and epiphysal slipping, in which the histopathologic appearance of the bone is similar

I suggest, therefore, that in a case of traumatic dislocation of the hip the reduction should be effected by the gentlest measure that will return the femoral head into the acetabulum. If great manipulative force is necessary it may be better to reduce the dislocation by open operation, in which only gentle handling would serve to replace the head. In this detail there is a precedent in the treatment of congenital dislocations of the hip, for which one now never uses great force. After the reduction and immobilization one should keep the patient in bed for several weeks to allow the irritation incidental to the trauma of the dislocation to subside. One should then apply a Thomas caliper brace. The brace should be somewhat too long in order to assure lack of weight bearing through the hip. Furthermore, a well fitting ischial ring should be attached, so that all of the weight on the affected side may be transmitted through the ischium. This brace should be worn for a year or even longer, until there is complete reformation of the femoral head in outline and especially in texture. The brace must not be removed until the substance of the femoral head has the quality of the adjacent bone. In the meantime, physical therapy (baking, massage, hydrotherapy and active and passive exercises) may be utilized to aid return of normal function.

SUMMARY

Two cases are reported in which in a young adult after a traumatic dislocation of the hip the top of the femoral head underwent aseptic necrosis. This lesion resulted from interruption of the blood supply through the ligamentum teres, which was ruptured during the dislocation. The necrotic process was exaggerated by too early weight bearing, which caused crushing of the devitalized bone. Secondary synovitis set in with increase in the synovial fluid and formation of a pannus on the neck of the femur. Some osteophytes appeared on the femoral head at its junction with the neck, representing undoubtedly an attempt at repair. The articular cartilage was seriously damaged, macroscopically it was found to be eroded, elevated from the underlying bone and even reduced to tabs or shreds, microscopically it showed extensive hyaline degeneration. The pathologic process resulted in what appeared clinically as arthritis with flexion and adduction deformity of the hip and severe limitation of its function. This experience in my cases and in those reported by other observers leads me to the conclusion that less damage would be incurred and an opportunity for better anatomic and functional result would be provided in this type of injury no weight bearing were allowed until complete healing, as evidenced roentgenographically by normal bony structure in the femoral head, has occurred.

TUMORS OF THE SMALL INTESTINE

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Tumors of the small intestine are not medical curiosities, yet it is rare to find more than a paragraph or two devoted to this subject in the average textbook on surgery. A search through the literature reveals that hundreds of cases have been reported, and it is a small hospital that does not have several examples among its records. What, then, is the reason for this relative obscurity? In the first place, tumors of other parts of the gastrointestinal tract occur more frequently, hence they are deserving of primary recognition. Secondly, the diagnosis of tumor of the small intestine is made with difficulty, as a matter of fact, the disease is often first recognized during an operation performed for the relief of a complication. The purpose of this paper will be well served if it results in a proper evaluation of the clinical importance of this group of diseases.

In 1919, Judd¹ stated that a number of clinics had reported finding 3 per cent of intestinal carcinomas in the small bowel, although the 24 cases which he described formed a much smaller incidence. Ewing² also estimated the frequency of malignant tumors of the small intestine at 3 per cent of all found in the gastrointestinal tract. Rankin and Mayo³ reported that up to 1929 there were 55 cases of carcinoma of the small intestine at the Mayo Clinic, as compared with 4,597 cases of carcinoma of the large intestine and rectum and 4,335 cases of carcinoma of the stomach. Raiford,⁴ in his excellent review of the

From the surgical service of Dr Cohn and from the private practice of Dr Cohn and Dr Landy at the Bronx Hospital.

1 Judd E S. Carcinoma of the Small Intestine. *Journal-Lancet* **39** 159, 1919.

2 Ewing J. *Neoplastic Diseases*. Philadelphia, W B Saunders Company, 1928.

3 Rankin F W and Mayo C. Carcinoma of the Small Bowel, *Surg, Gynec & Obst* **50** 939 1930.

4 Raiford T S. Tumors of the Small Intestine, *Arch Surg* **25** 122 (July) 1932.

subject, pointed out that in a series of 986 tumors of the intestinal tract at the Johns Hopkins Hospital, 88 tumors, or 8.9 per cent, were in the small bowel. In his series there were 776 malignant tumors, of which 38, or 4.9 per cent, were situated in the small intestine. There were 210 benign tumors, of which 50, or 23.8 per cent, were located in the small bowel. These figures show that both types of tumor are more frequent in the large intestine and in the stomach, but in the small intestine tumors are predominantly benign, while in other parts of the gastrointestinal tract they are predominantly malignant.

MALIGNANT TUMORS

Carcinoma—Carcinoma is one of the most frequently encountered malignant tumors of the small intestine. In most reported series it is found in approximately 3 per cent of the total number of carcinomas of the gastrointestinal tract. In the Mayo Clinic series the average age of the patients was 47.5 years. The growth occurs twice as often in males as in females.

Most observers agree that the duodenum is the most frequent site of carcinoma of the small bowel. In Rarford's series 8 of 16 tumors were in the duodenum. Rankin and Mayo, however, stated that 21 of the 55 tumors described by them were in the jejunum. Considering the relative shortness of the duodenum, the frequent finding of carcinoma there is noteworthy. If the duodenum is divided into three parts, namely, preampullary, perampullary and prejejunal, the perampullary region is undoubtedly the most frequent site of carcinoma. This explains the frequency of involvement of the ampulla of Vater.

The most usual types of carcinoma of the small intestine are adenocarcinoma and medullary carcinoma. The growths are most often on the annular or constricting form, but polypoid and ulcerative infiltrating growths are also seen. Adenocarcinoma is easily recognized microscopically by its atypical glandular formation and infiltrating malignant cells. Medullary carcinoma is highly malignant. It develops from the epithelium of the mucosa but shows no tendency toward glandular formation. It is a fungating tumor, bleeding easily, and often first calls attention to itself by hemorrhage.

Carcinoma of the small intestine metastasizes early, and metastases are found in about one third of the cases at the time of operation. The sites of metastasis in the order of frequency are mesenteric lymph nodes, peritoneum, liver, lungs and long bones.

It is interesting to conjecture why the small intestine, which is much longer than the stomach and large intestine combined, is much less frequently the site of carcinoma. Rankin and Mayo suggested that the alkalinity and fluidity of the contents of the small bowel, as well as the absence of abrupt bends, may be the expla-

Sarcoma—Sarcoma of the small intestine occurs often enough to deserve widespread recognition. In 1934 Boyce and McFetridge⁵ collected over 300 cases from the literature. In an earlier study Corner and Fairbank⁶ reviewed 103 cases of sarcoma of the intestinal tract and found that 63 per cent of the tumors were in the small intestine, the largest number being in the ileum. We differentiate here the true sarcoma from the lymphosarcoma, which is better termed "lymphoblastoma" to avoid confusion.

Ewing stated that a sarcoma may arise from any mature mesoblastic tissue, which in the small intestine includes the submucosa, the subserous connective tissue and the muscular coats of the intestinal wall. Histologically this accounts for the finding of fibrosarcoma and leiomyosarcoma as the most frequent types of sarcoma of the small bowel.

Lymphoblastoma, or lymphosarcoma, is one of the most frequently encountered malignant tumors of the small intestine. The extensive lymphatic development of the small bowel probably renders it peculiarly susceptible to this disease. Ullman and Abeshouse,⁸ in 1932, in a comprehensive review of lymphosarcoma of the intestinal tract, brought the total number of reported cases up to 375. Lymphoblastomas occur at any age but are especially frequent in the fourth and fifth decades of life. A large proportion of them are found in the terminal portion of the ileum.

BENIGN TUMORS

Adenoma—The simple adenoma is the most frequently found benign tumor of the small intestine. In Raitord's series there were 15 adenomas, 10 of which were located in the ileum. Histologically the adenoma consists of soft masses of glandular tissue with a connective tissue stroma which is probably derived from the submucosa. The glandular tissue shows no evidence of malignant change, and its continuity with the normal mucosa can readily be traced.

Adenomas are usually single and small, but they sometimes occur in great numbers as in multiple polyposis.⁹ In most cases the adenoma is not of great clinical significance except when it is the cause of

⁵ Boyce F F and McFetridge E M. Primary Sarcoma of Intestine. *Internat S Digest* **17** 131 1934.

⁶ Corner E M and Fairbank H A T. Sarcomata of the Alimentary Tract. *Tr Path Soc London* **56** 20 1905.

⁷ Mayo C W and Robins C R Jr. Lymphosarcoma. *S Clin North America* **15** 1163 1935.

⁸ Ullman A and Abeshouse B S. Lymphosarcoma of Small and Large Intestine. *Ann Surg* **95** 878 1932.

⁹ Gatersleben H. Polyposis of Small Intestine. *Deutsche Ztschr f Chir* **245** 628 1935.

obstruction, intussusception or hemorrhage. Divergent theories are held as to the origin of adenomas, that is, as to whether they are the result of inflammatory changes or are primarily neoplastic. Although it seems well established that malignant disease frequently complicates multiple polyposis, it is debatable whether malignant changes can occur in the simple adenoma.

Fibroma—Fibromas¹⁰ are extremely rare in the small intestine, there being fewer than 40 reported cases in the literature. They arise from the submucosa or from the subserous connective tissue. While a few such tumors have occurred in children, the great majority of them have been found in persons in the fifth and sixth decades. Fibromas are usually small and rarely cause symptoms.

Leiomyoma—Leiomyomas are among the more frequently reported tumors of the small intestine. They are found in the small and large bowel with equal frequency. King¹⁰ collected 45 cases from the literature in 1917, but many more have been described since that time. They occur at all ages. In the small intestine the most frequent site is the ileum and the next most frequent the jejunum. They occur least often in the duodenum.

Leiomyomas usually develop from the internal or external muscular coats of the intestinal wall. Theoretically, they may arise also from the muscularis mucosae and from the arterioles, but this has not been established. They form predominantly internal or external tumors with reference to the lumen. They are slowly growing, but they may develop into huge masses. Histologically, leiomyomas consist of whorls of hypertrophied smooth muscle cells arranged in interlacing bundles supported by a connective tissue framework. They have a tendency toward hemorrhagic degeneration, which accounts for the frequent bleeding associated with the condition.

Lipoma—Lipomas¹¹ are seldom seen except incidentally at the operating table or at necropsy. They are notable for their benign and innocuous nature, but occasionally their surfaces may become ulcerated and extensive bleeding may result. Microscopically, they reveal masses of the adult type of fat cells surrounded by delicate strands of connective tissue. Spontaneous expulsion of pedunculated lipomas has been reported.

Hemangioma—Hemangiomas of the small intestine are rare but interesting tumors. Helvestine¹² described 14 cases found in the liter-

¹⁰ King, E. L. Benign Tumors of the Small Intestine, Surg. Gynec. & Obst. 25 54, 1917.

¹¹ Comfort, M. W. Submucous Lipomata of the Gastrointestinal Tract, Surg., Gynec. & Obst. 52 101, 1931.

¹² Helvestine, F., Jr. Hemangiomatosis of the Intestines, Ann. Surg. 78 42 1923.

ture and 1 of his own. These tumors arise from blood vessels in the submucosa. Histologically they are composed of endothelium-lined spaces filled with blood and fibrin and supported by a connective tissue framework. They are described as being capillary or cystic, depending on the size and caliber of the vessels involved. They are of interest clinically because they may cause extensive and uncontrollable hemorrhage. Bleeding high in the small intestine may simulate a bleeding peptic ulcer¹³ while bleeding in the lower portion of the small intestine may arouse suspicion of a malignant growth.

Chylangiomas¹⁴ are similar to hemangiomas in histologic structure except that instead of containing blood and fibrin they are filled with a gelatinous, pink-staining material derived from lymph. They originate from the lymphatic plexus of the submucosa.

Carcinoid or Argentaffin Tumor—The occurrence of carcinoid tumors in the small intestine has frequently been described. The report by Cooke¹⁵ on this subject should be consulted. These tumors resemble carcinoma superficially but differ in these important respects. They show no intracellular changes; they have no tendency toward glandular formation and they do not metastasize. They are not of great interest clinically because of their small size, being rarely more than 1 or 2 cm in diameter. Large carcinoids have been found in the appendix.

Rare Tumors—Aberrant pancreatic rests¹⁶ are tiny benign tumors, 1 or 2 cm in diameter, which receive their name from the fact that their histologic picture is strikingly similar to that of normal pancreas except that islands of Langerhans may be absent. It is probable that they develop from misplaced embryonal tissue.

Intestinal cysts are occasionally reported but they are extremely rare. We distinguish here between true intestinal cysts and mesenteric cysts, which are not infrequent. Cystic pneumatosis¹⁷ is a condition found in the Orient. In this disease gas-filled cysts of varying size are found due to penetration of intestinal gas through tiny weak points in the bowel wall. The condition subsides spontaneously if let alone.

13 Dudley H. D. Vascular Tumors of Small Intestine with Symptoms Simulating Peptic Ulcer. *S. Clin. North America* **14**: 1331, 1934.

14 Naumann H. Chylangioma Cavernosum and Cysticum of the Ileum, *Arch. f. klin. Chir.* **147**: 314, 1927.

15 Cooke H. H. Carcinoid Tumors of the Small Intestine. *Arch. Surg.* **22**: 568 (April) 1931.

16 Simpson W. M. Aberrant Pancreatic Tissue. Analysis of One Hundred and Fifty Human Cases with Report of a New Case, in *Contributions to Medical Science Dedicated to Aldred Scott Warthin*. Ann Arbor, Mich. George Wahr, 1927, p. 435.

17 Bubis I. L. and Swanbeck C. E. Gas Cysts of the Intestine. *Ann. Surg.* **75**: 620, 1928.

All types of benign and malignant tumors of Meckel's diverticulum have been reported, but they are obviously rare. Nygaard and Walters¹⁸ collected 17 cases from the literature and added 3 of their own.

Secondary Tumors—The small intestine is often involved in malignant tumors, which may originate in the stomach, colon, ovary or other abdominal organ. This involvement may be by direct extension or by metastasis.

CLINICAL ASPECTS

As we have mentioned, the diagnosis of tumor of the small intestine is made with difficulty. Often the finding of this condition at the operating table comes as a complete surprise to the surgeon. In reviewing a case the surgeon will frequently find that the clinical signs had pointed definitely to a disease of the small intestine but had not been so interpreted because of the relative infrequency of such a condition and the confusing similarity of the symptoms to those of other abdominal diseases. We believe that if the existence of this condition is kept in mind a correct diagnosis can be made in a fair percentage of cases.

The symptoms and clinical signs of the disease are due to changes in the mechanics of gastrointestinal function resulting from the presence of the tumor and also to the effect of the pathologic process on the general condition of the patient. In general, the symptoms vary according to the location of the tumor, its type, whether benign or malignant, and, in the latter instance, the degree of malignancy. The location and effect of metastases also play a part in the disease picture.

The symptoms are usually those of intestinal obstruction and may be acute, chronic or intermittent. It must be kept in mind, however, that a complication, such as perforation or hemorrhage may be the first indication of the existence of the disease. Pain is the most frequent complaint, it is colicky and may be mild or severe. Nausea and vomiting are often present, especially in cases of tumor of the duodenum, if the tumor is in the jejunum or the ileum these symptoms appear later. There is often a loss of weight and strength, which is more marked if the tumor is malignant. There may be a change in intestinal habits, such as alternating attacks of diarrhea and constipation.

In the absence of complications there are few clinical findings on physical examination. The most frequent findings on palpating the abdomen are tenderness and a sensation of fulness to the examining finger. In a small proportion of cases there is a definite mass, which constitutes the most valuable single sign of tumor. Distention of the abdomen may be present. A succussion splash may be elicited. Barium

18 Nygaard, K. K., and Walters, W. Malignant Tumors of Meckel's Diverticulum, Proc. Staff Meet., Mayo Clin. 11: 504, 1936.

gross or occult may be present in the stool or vomitus. In cases in which there is frequent vomiting, such as occurs with tumors high in the small intestine, dehydration and alkalosis are present, as well as hypochloremia and nitrogen retention. In periampullary tumors, jaundice simulating that associated with carcinoma of the head of the pancreas may be present.

With the onset of intestinal obstruction there arises the familiar picture of pain, distention, vomiting, constipation and perhaps visible peristaltic waves and signs of shock. When intussusception is present (and we must emphasize the frequent complicating of these tumors by intussusception¹⁹) one may find pain, characterized by sudden onset, accurate localization and long duration if not relieved, vomiting and the appearance of an elongated mass. Bloody stools may be passed.

Cases in which there is a gradual development of symptoms indicative of intestinal disturbance offer the surgeon sufficient time to make a correct diagnosis. In other cases, in which one is confronted with obvious peritonitis without sufficient antecedent history to make a correct diagnosis, the signs may point to appendicitis, perforated or bleeding ulcer or cholecystitis and may tax the diagnostic skill of the surgeon to the utmost.

Roentgenograms are not as helpful in cases of tumor of the small intestine as they are in cases of tumor elsewhere, on account of the great length of the intestine and the difficulty of filling it homogeneously. However, the finding of dilatation, filling defects, indentations due to constriction or evidences of acute or chronic obstruction offers assistance to the diagnostician.²⁰ Negative results from roentgen examination do not rule out tumor of the small intestine, but positive results are of definite value.²¹

19 Fiske, F. A. Intussusception Due to Intestinal Tumors, *Ann Surg* **106** 221, 1937.

20 Soper, H. W. Roentgen Ray Diagnosis of Lesions of the Small Intestine, *Am J Roentgenol* **22** 107, 1929.

21 Ackerman, L. V. Cavernous Hemangioma of the Small and Large Bowel, *Am J Cancer* **30** 753, 1937. Rankin, F. W., and Grimes, A. E. Small Bowel Tumors, *South Surgeon* **6** 280, 1937. Nickerson, D. A., and Williams, R. H. Malignant Tumors of the Small Intestines, *Am J Path* **13** 53, 1937. Liccione, W. T. Malignant Tumors of Meckel's Diverticulum, *Am J Surg* **34** 103, 1936. Doub, H. P., and Jones, H. C. Primary Malignant Tumors of the Small Intestine, *Radiology* **26** 209, 1936. Klopp, E. J., and Crawford, B. L. Leiomyoma of the Small Intestine, *Ann Surg* **101** 726, 1935. Kirshbaum, J. D. Submucous Lipomas of the Intestinal Tract as Cause of Intestinal Obstruction, *ibid* **101** 734, 1935. Joyce, T. M. Tumors of the Small Intestine, *ibid* **100** 949, 1934. Moore, R. H., and Schmeisser, H. C. Benign Tumors of the Small Intestine, *South M J* **27** 386, 1934. Prev, D., Foster, J. M., Jr. and Dennis, W. Primary Sarcoma of the Duodenum. Report of a Case, *Arch Surg* **30** 675 (April) 1935.

REPORT OF CASES

CASE 1—M. T., a 50 year old white woman, was admitted to the surgical service on Sept. 14, 1932, with the complaint of generalized abdominal pains of several hours' duration. She had not had any previous serious illness or operation. Four months previously she had begun to have attacks of abdominal distress without any real pain. A series of gastrointestinal roentgenograms at that time revealed no abnormality. Six hours before her admission to the hospital she was suddenly seized with sharp, cramplike generalized pains, most severe in the right lower quadrant of the abdomen. She was nauseated and vomited several times. There had been two normal bowel movements during the previous twenty-four hours.

Physical examination revealed the patient to be acutely ill. The temperature was 100.2 F., the pulse rate 64 and the respiratory rate 20. The upper respiratory passages, lungs and heart were normal. The abdomen was moderately rigid on both sides but was more so on the right, there were definite localized tenderness and rebound tenderness in the right lower quadrant. No masses could be felt. The leukocyte count was 11,200 per cubic millimeter, with 88 per cent polymorphonuclears and 12 per cent lymphocytes. Urinalysis revealed traces of albumin, occasional white blood cells and no casts.

On the basis of these findings a diagnosis of acute appendicitis was made.

The abdomen was opened through a lower right rectus incision with the patient under general anesthesia. A large amount of fluid and clotted blood was encountered, which was easily traced to a ruptured cystic mass attached to the ileum. Exploration revealed no involvement of the lymph nodes, and the viscera appeared free of metastasis. A resection of the involved loop of ileum was made, and a side to side anastomosis was performed.

The patient reacted well from the operation, and her subsequent course in the hospital was uneventful. She was discharged on the twentieth day after the operation.

Pathologic Report—Gross Picture. The specimen consisted of numerous fragments of clotted blood and soft papillary tissue, some of which was free and much of which was attached to what appeared to be the wall of a cyst measuring approximately 7 by 5 cm. There was also submitted a small portion of ileum to which some papillary material, similar to that previously described, was attached on its peritoneal surface.

Histologic Picture. The tumor was cellular, with a somewhat hyaline stroma. The cells were essentially oval, with hyperchromatic nuclei and many atypical giant forms. Many mitotic figures were present, some of them multipolar. The diagnosis was leiomyosarcoma.

Forbus, W. D. Argentaffin Tumors of the Appendix and Small Intestine, *Bull. Johns Hopkins Hosp.* **37** 130, 1925. Ritter, S. A. Neuroblastoma of the Intestine, *Am. J. Path.* **1** 519, 1925. Bier, E. Lymphosarcoma of the Small Intestine, *S. Clin. North America* **5** 93, 1925. Rankin, F. W. Lymphosarcoma of the Small Intestine, *Ann. Surg.* **80** 704, 1924. Clark, E. D. Carcinoma of the Small Intestine, *Surg., Gynec. & Obst.* **43** 757, 1926. Brown, A. J. Vascular Tumors of the Intestines, *ibid.* **39** 191, 1924. Judd, E. S., and Rankin, F. W. Hemangiomas of the Gastrointestinal Tract, *Ann. Surg.* **76** 28, 1922. Mills, R. V. Radiological Diagnosis of Small Intestinal States, *Am. J. Roentgenol.* **9** 199, 1922. Goldsmith, R. Leiomyosarcoma of the Jejunum, *Ann. Surg.* **101** 14, 1935. Charache, H. Primary Lymphosarcoma, *Am. J. Surg.* **27** 171, 1935.

Follow-Up—Examinations of the patient at intervals of six months have revealed no recurrence of the tumor. She was alive and well when last seen, one year prior to the time of writing.

CASE 2—T. B., a 32 year old white woman, was admitted to the hospital on July 11, 1933, with the complaint of abdominal pains of one week's duration. Prior to the onset of the illness for which she sought admission she had always enjoyed good health. A week previously she had pains of moderate intensity in the lower portion of the abdomen. These persisted until the day of admission, when they

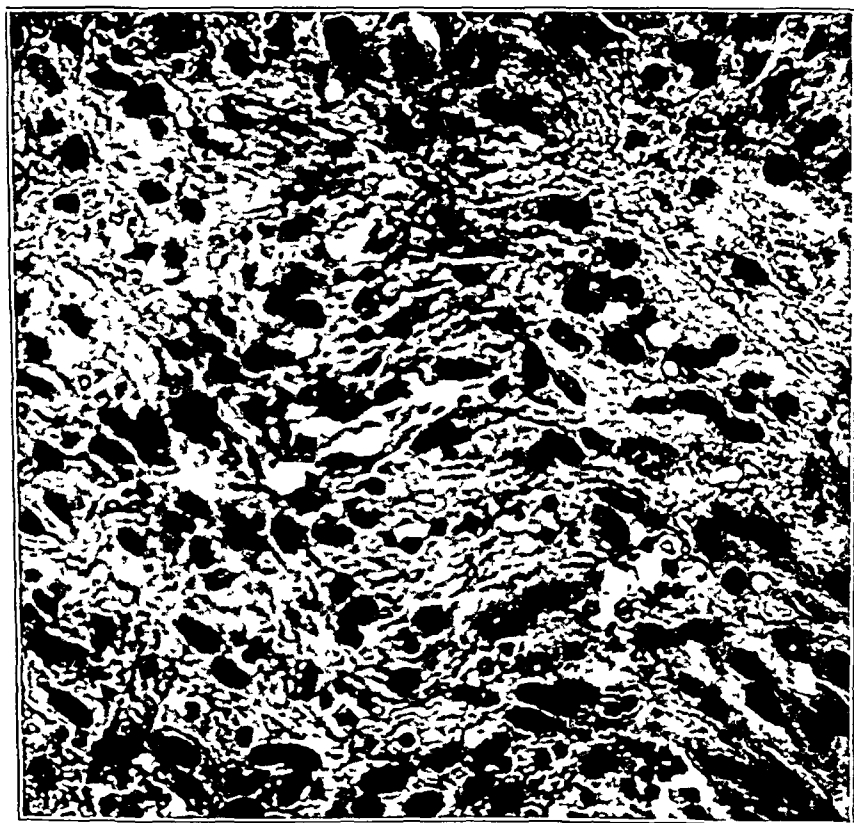


Fig. 1—Leiomyosarcoma

became more severe and seemed to localize in the right lower quadrant. She became nauseated and vomited frequently.

On examination the patient appeared acutely ill. The temperature was 104 F., the pulse rate 104 and the respiratory rate 24. Examination of the throat, lungs and heart revealed no abnormalities. Palpation of the abdomen revealed spasticity of both rectus muscles, especially of the right, and there was considerable distention. No masses could be felt. The leukocyte count was 9800 per cubic millimeter with 84 per cent polymorphonuclears and 16 per cent lymphocytes. Urinalysis revealed no abnormalities.

A tentative diagnosis of pelvic peritonitis, possibly due to adnexal disease, was made. The possibility of appendicitis was also considered. Supportive treatment for the purpose of localizing the peritonitis was instituted. However, the patient's condition became steadily worse during the next two days, and operative intervention was decided on.

With the patient under general anesthesia, a lower right rectus incision was made. When the peritoneal cavity was entered a large amount of purulent fluid was encountered. Exploration revealed a large, necrotic tumor of the ileum. The



Fig 2—Leiomyosarcoma

appendix and adnexae were inflamed by contiguity. A resection of the involved loop of ileum was made, followed by an end to end anastomosis. The appendix was removed. The abdominal cavity was drained and closed.

The postoperative course was stormy during the next few days, but after a blood transfusion the patient improved steadily. She was discharged on the twenty-fifth day after the operation with the wound completely healed.

Pathologic Report—Gross Picture. The specimen consisted of an irregular, somewhat conical mass 8 by 6 cm. The base was nodular and the area hemorrhagic, the remainder becoming whitish and interspersed with opaque areas. On cut section this appeared to be a well encapsulated

tumor, the middle third being occupied by soft, reddish tissue. There were some areas which were yellowish and translucent.

Histologic Picture There were marked proliferation, hyperchromatism and many variations in size of the cells. The general appearance of the cells suggested the whorls seen in uterine leiomyomas. Many atypical cell forms, however, were present, with evidence of very rapid cell division and some necrosis. The diagnosis was leiomyosarcoma.

Follow-Up—The patient was last seen six months prior to the time of writing and has remained well. There has been no evidence of recurrence.

CASE 3—S. S., a 21 year old white man, was admitted to the medical service of Dr. S. P. Sobel on Dec. 3, 1935, with the complaints of shortness of breath and attacks of abdominal pains. There was no previous history of rheumatic fever. For the past eighteen months he had suffered attacks of abdominal pains associated with nausea and vomiting, which were not related to eating and were not relieved by medication. Recently the attacks had become more frequent and had lasted for days at a time. During the past year he had become aware also of increasing shortness of breath on exertion.

Physical examination revealed the patient to be orthopneic and cyanotic. The superficial veins were congested. The pulse showed auricular fibrillation, with a rate of about 112 beats per minute. The blood pressure was 124 systolic and 42 diastolic. The lungs showed dulness at both bases on percussion, and many moist rales were audible. The heart was enlarged along both borders and over the mitral valve both systolic and diastolic murmurs were heard. A diastolic murmur was heard also over the aortic area. The liver was enlarged to 2 finger-breadths below the costal margin. No masses were felt in the abdomen. There was slight pitting edema of the lower extremities. The Wassermann and Kahn reactions were negative. The blood count and urinalysis revealed no abnormality.

A diagnosis was made of rheumatic heart disease with mitral and aortic valvular involvement, auricular fibrillation and myocardial failure. This was confirmed by electrocardiographic and roentgen examinations.

The patient was rapidly digitalized and made satisfactory progress during the next few days. One week after admission he was suddenly seized with an attack of cramplike abdominal pains. Examination of the abdomen showed that the liver had receded in size, but in the right lower quadrant there was a soft, tender, elongated mass. There was no fever and the leukocyte count was 8,800, with a normal differential count. A series of gastrointestinal roentgenograms showed incomplete obstruction. Several diagnoses were offered, including mesenteric vascular thrombosis, volvulus, appendicitis and intussusception. After several days of observation the attack subsided spontaneously and was followed by several similar attacks of lesser intensity. Finally a severe attack occurred, with the appearance of a long, sausage-shaped mass in the right lower quadrant of the abdomen. On the basis of the recurrent nature of the attacks with the presence of the gradually extending mass a diagnosis of ileocecal intussusception, probably caused by a tumor of the ileum, was made.

With the use of spinal anesthesia a right rectus incision was made. A large intussusception of the ileum through the ileocecal valve was found. This was carefully reduced and the cause of the intussusception was found to be a pedunculated, ball-like tumor situated about 18 inches (45 cm.) from the cecal end of the ileum. The tumor-bearing portion of the ileum was resected and a side to side anastomosis created.

The patient made an uneventful recovery and on the twenty-sixth day after operation was transferred from the hospital to a home for convalescent patients with cardiac disease

Pathologic Report—*Gross Picture* The specimen consisted of a resected portion of intestine, 10 cm in length, apparently ileum. On the mucosal aspect there was an eccentrically situated tumor, 4 cm in its largest diameter and roughly oval. It had a short, thick pedicle. The serosal aspect at the site of the tumor

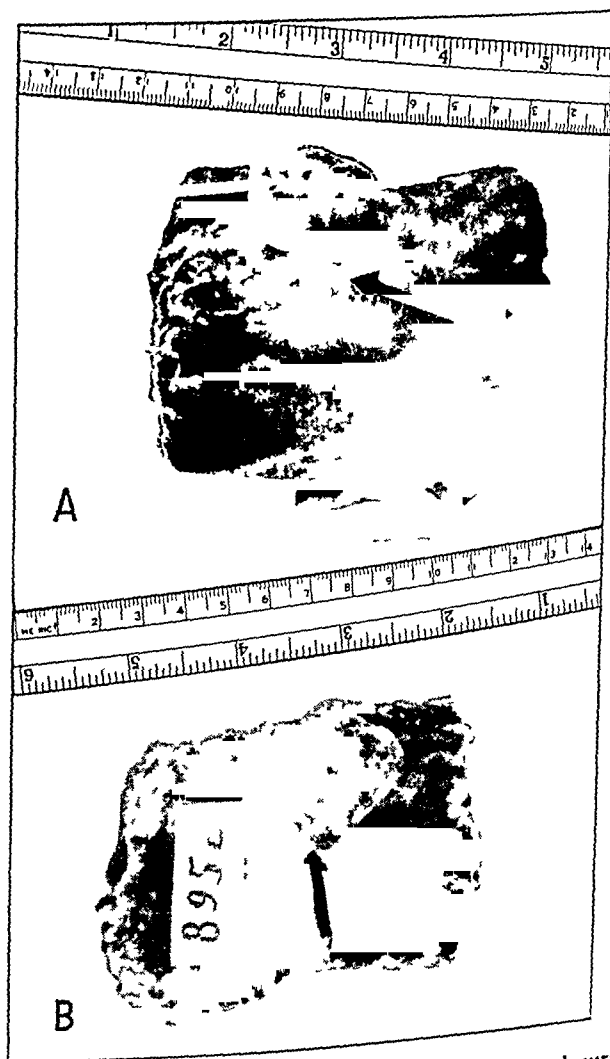


Fig 3—A, serosal surface of a leiomyoma. B, mucosal surface

mass showed a peculiar puckering and several small nodules, 2 to 4 mm in diameter.

Histologic Picture The cells consisted of elongated oval to spindle-shaped cells with slightly hyperchromatic nuclei embedded in a rather dense, edematous stroma. There appeared to be no evidence of rapid cell division or other features pointing to malignancy. The diagnosis was leiomyoma.

Follow-Up—The patient has been seen within recent months and her cardiac condition is still in evidence; there has been no recurrence of abdominal symptoms.

CASE 4—R E a 23 year old white man, was admitted to the hospital on Nov. 22 1936, with the complaint of generalized abdominal pains associated with nausea and vomiting. One year ago he had begun to have attacks of diarrhea accompanied by mild cramplike pains. These aroused no anxiety, and he gained several pounds in weight during this time. One week before admission he was seized with an attack of severe pains near the umbilicus. The following day diarrhea appeared, lasting twenty-four hours. After this he felt better except for mild pains which recurred at intervals. On the day prior to admission severe intermittent colicky pains again appeared, with nausea and vomiting.



Fig. 4—Leiomyoma

The temperature on admission was 100.6 F, the pulse rate 68 and the respiratory rate 22. Examination of the nose and throat revealed no abnormalities. The lungs were clear to percussion and auscultation. The heart was normal. The abdomen was considerably distended, but no tenderness or rigidity was noted. No masses were felt. The leukocyte count was 10,700 per cubic millimeter, with band forms 8 per cent, polymorphonuclears 74 per cent, lymphocytes 16 per cent and monocytes 2 per cent. Urinalysis revealed no abnormalities. Roentgenograms showed marked gas distention of the small bowel mainly in the left upper quadrant of the abdomen, with the patient in the erect posture. Fluid levels were present. The stomach was distended and contained fluid. A diagnosis of intestinal obstruction high in the small bowel was made.

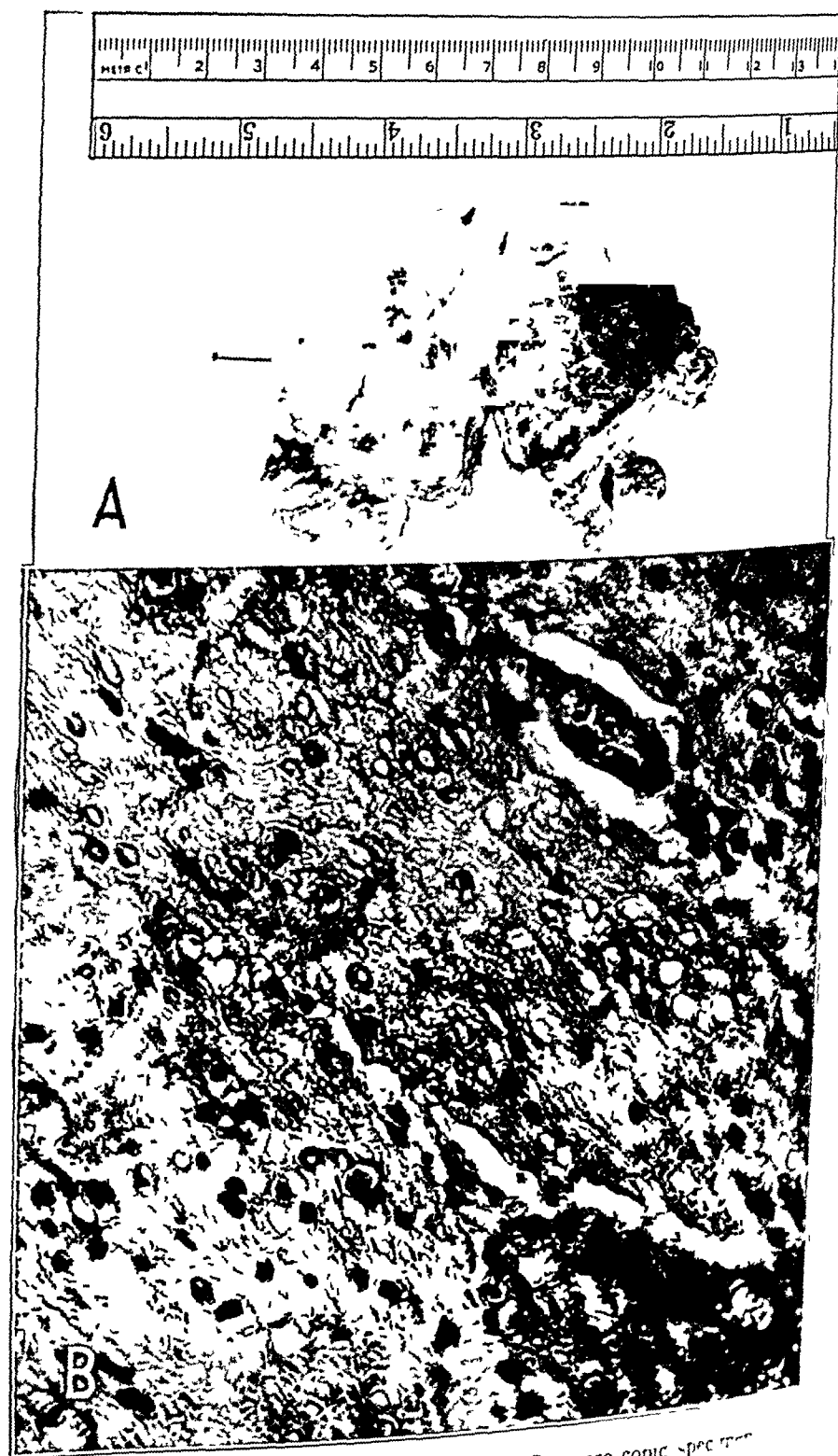


Fig 5—Leiomyoma *A*, gross specimen, *B*, microscopic specimen

With the use of spinal anesthesia a left upper rectus incision was made. When the peritoneal cavity was entered a large amount of serosanguineous fluid was encountered and distended loops of small intestine were seen. An oval tumor about the size of a golf ball was found attached to the upper portion of the ileum at the antimesenteric border by a narrow pedicle. The tumor was hemorrhagic and somewhat necrotic. It had rotated four times on its pedicle. There was an acute angulation of the bowel due to the pulling up of the tumor by adherent omentum, and this was the mechanism of the obstruction. The tumor was easily removed by clamping and ligating the base of the pedicle, and the serosal surface was covered over by a Lembert suture.

The patient made an uneventful recovery and was discharged from the hospital on the fourteenth day after the operation.

Pathologic Report—Gross Picture The specimen consisted of a pedunculated tumor mass 4 by 4 cm, attached to the mucosal aspect of the small intestine by a 2 cm pedicle. The mass appeared well encapsulated and was firm. On section it was hemorrhagic in appearance, and the pedicle contained a small lumen. A small portion of the omentum was attached to the tumor. The general appearance suggested torsion and strangulation.

Histologic Picture The appearance was that of degeneration with hemorrhagic infiltration of leiomyoma. The pedicle consisted of intestinal wall devoid of mucosa. There was a lumen in the pedicle, not lined by epithelium. The diagnosis was degenerated leiomyoma.

Follow-Up—The patient was last seen three months prior to the time of writing and showed no evidence of recurrence.

CASE 5—R. N., a 30 year old white woman, was admitted to the hospital on Sept. 30, 1932, with the complaint of frequent attacks of abdominal pains associated with nausea and vomiting. These attacks had begun six months previously and had been infrequent at first but recently had become a daily occurrence. Since the onset of this illness she had lost 20 pounds (9.1 Kg.).

On physical examination the patient looked emaciated and chronically ill. The temperature was 101.2 F., the pulse rate was 120, and the respiratory rate was 22. Examination of the upper respiratory passages, the lungs and the heart revealed no abnormalities. The abdomen had a peculiar doughy resistance on palpation. On deep palpation there was slight tenderness in the right lower quadrant. No masses could be felt. No fluid wave was present. Vaginal examination showed the uterus to be retroverted, and the cervix revealed chronic endocervicitis. Laboratory examination revealed hemoglobin, 73 per cent, leukocytes, 11,500 per cubic millimeter, with polymorphonuclears 77 per cent and lymphocytes 23 per cent. The urine was normal. Roentgenograms of the chest and a flat plate of the abdomen revealed no abnormalities. A series of cholecystograms showed that the gallbladder filled faintly with dye, probably owing to adhesions between it and the duodenum. No stones were present.

On the basis of these findings it was suspected that chronic peritonitis, possibly tuberculous, was present, and exploratory operation was advised.

Laparotomy was performed with the use of spinal anesthesia. A tumor mass was found attached to the upper portion of the jejunum about 9 inches (23 cm.) from the fossa of Treitz. The omentum was adherent to the tumor. The mesenteric lymph nodes were enlarged but the liver and other viscera appeared to be free of metastasis. A resection of the involved jejunum including about 3 inches (7.5 cm.) on either side of the tumor was performed and the continuity of the intestine was restored by a side to side anastomosis.

The patient made an uneventful recovery from the operation and was discharged on the fifteenth postoperative day.

Pathologic Report—Gross Picture The specimen consisted of a 10 cm portion of small intestine exhibiting on its mucosal aspect a solid oval tumor, approximately 3 by 2.5 cm. The mass was sessile and appeared to have penetrated the entire wall, involving a small mass of fat which was adherent to its serosal surface.

Histologic Picture The cells consisted essentially of spindle and oval types, varying in size and exhibiting many degrees of polymorphism, hyperchromatism, giant nuclei and atypical mitosis. There was a fine connective tissue stroma which appeared to be well vascularized. The diagnosis was leiomyosarcoma.

Second Admission—On August 29, 1937, five years after her discharge, the patient was readmitted. She stated that she had been well until six weeks previously, when attacks of abdominal pain accompanied by vomiting had returned. Her weight, which had increased from 101 to 128 pounds (46 to 58 Kg) during this time, had fallen to about 113 pounds (51 Kg) during the few weeks just past. She felt continually nauseated.

Physical examination gave essentially negative results except for the abdomen. On palpation the abdomen was distended and markedly tender. Irregular masses could be felt in the left lower quadrant. A diagnosis of subacute intestinal obstruction due to a recurrence of the tumor was made. After a week of observation with no amelioration of symptoms a blood transfusion was given. The following day exploratory operation was performed. A large, conglomerate mass of intestines was found, which was the seat of widespread sarcomatous involvement. Intervention was deemed inadvisable.

The patient rallied from the operation, but on the following day the temperature became elevated and signs of consolidation appeared at the bases of the lungs. The patient died on the third day after the operation.

CASE 6—S. R., a 9 year old girl, was admitted to the hospital on Aug 5, 1936, with the complaints of progressive enlargement of the abdomen and persistent fever. The child had been well until the onset of the present illness, three months previously. At that time the mother noticed that the abdomen was becoming progressively larger, although there were no subjective complaints. Ten days before her admission to the hospital there was a sudden increase in the enlargement and the child began to vomit. The temperature rose to 101 F. The next day the vomiting ceased, but the fever persisted. The patient became pale and lost considerable weight.

Physical examination revealed marked pallor, a temperature of 100 F, a pulse rate of 120 and a respiratory rate of 36. There was no enlargement of the superficial lymph nodes. There was dullness on percussion at the bases of the lungs with some diminution of the breath sounds. The heart was normal. Examination of the abdomen revealed marked distention and unusual prominence of the superficial veins. A large, irregular mass was palpable in the right lower portion of the abdomen. It was firm and could be displaced without pain. A fluid wave was present, with shifting dullness in the flanks. Laboratory examination showed closed hemoglobin, 70 per cent, erythrocytes, 4,300,000 per cubic millimeter, leukocytes, 14,000 per cubic millimeter, with band forms 10 per cent, polymorphonuclears 74 per cent, lymphocytes 13 per cent and monocytes 3 per cent. Urine was normal except for occasional red and white blood cells. Rectal examination revealed displacement of the ascending colon and cecum by a hard mass. Abdominal paracentesis was performed, and 1,000 cc of a light colored fluid was removed.

On the basis of these findings lymphosarcoma, Hodgkin's disease and malignant tumor of the right ovary were considered

Exploratory operation was performed with the patient under ether anesthesia. When the peritoneal cavity was entered it was necessary to evacuate about 6 quarts (5.6 liters) of turbid fluid. Several large tumor masses were encountered, the largest and apparently primary growth arising from the ileum. Several of these masses were amputated. The involved loop of bowel was delivered out of the wound and walled off with packing. As the condition of the patient suddenly

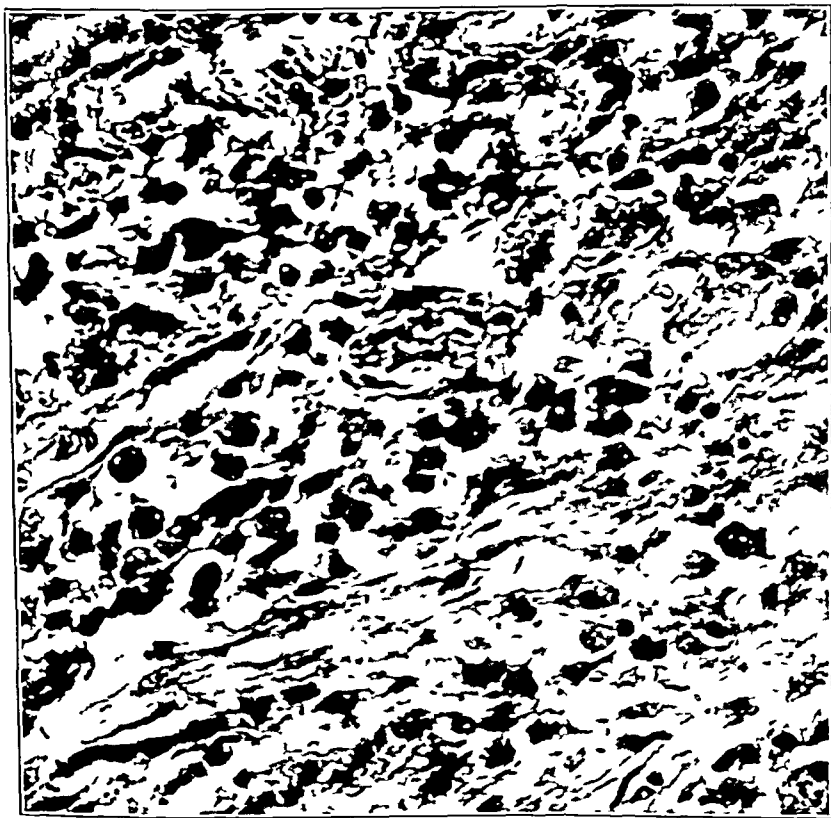


Fig 6—Leiomyosarcoma

became critical at this point the procedure was terminated with the expectation of resuming it later.

About an hour and a half after the operation the patient went into profound shock and died in spite of supportive measures.

Pathologic Report—Gross Picture. The specimen consisted of many irregular fragments of whitish tissue, the largest measuring 8 by 4 cm.

Histologic Picture. The sections exhibited a marked cellular proliferation, the type of cell being round with a large, pyknotic nucleus and scant, faintly staining cytoplasm. Many of the cells were large and exhibited evidence of rapid cell division. The stroma was scanty and in some places edematous. The diagnosis was lymphosarcoma.

CASE 7—E K, a 38 year old white woman, was admitted to the hospital on May 11, 1938, with the complaints of severe abdominal pains, nausea and vomiting for the past few hours. She stated that four months previously she had begun to have recurrent cramplike abdominal pains, especially in the left lower portion of her abdomen. She also became troubled by eructation, distention and increasing constipation. She vomited occasionally. Two weeks previously a barium sulfate enema had been given at another hospital and the results reported to be negative. A barium sulfate meal had been given also, but the report was not available. A few hours before admission she was suddenly seized with severe

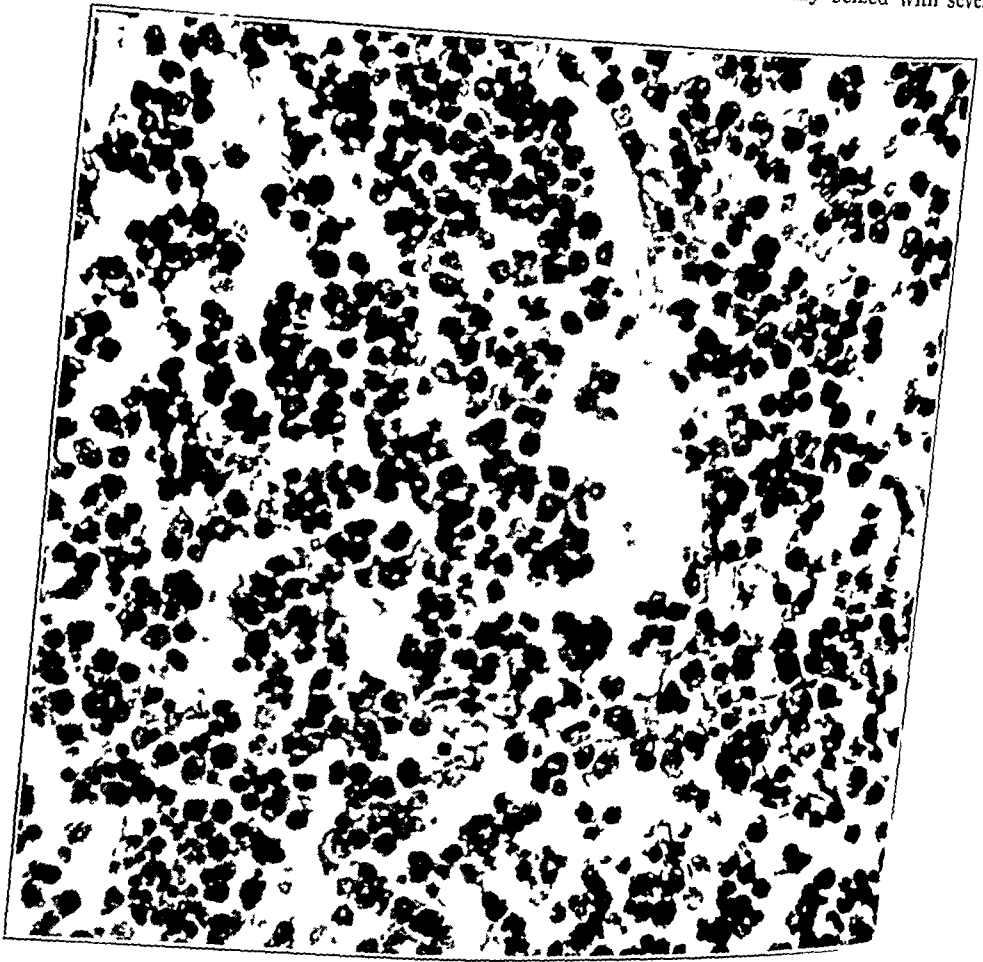


Fig 7—Lymphosarcoma

abdominal pains in the right lower quadrant, radiating upward toward the epigastrium and also felt in the back and in the right shoulder. She vomited during this time.

Physical examination revealed the patient to be acutely ill. The temperature was 99.6 F and the pulse rate 84. The heart and lungs were normal. The abdomen showed considerable distention, and there was rigidity of the abdominal muscles, especially on the right side. There was tenderness on palpation, with rebound tenderness, both more marked on the right side. Dulcness to percussion was not obliterated. Vaginal examination gave negative results. During the hospital examination there were recurrent exacerbations of the severe pain.

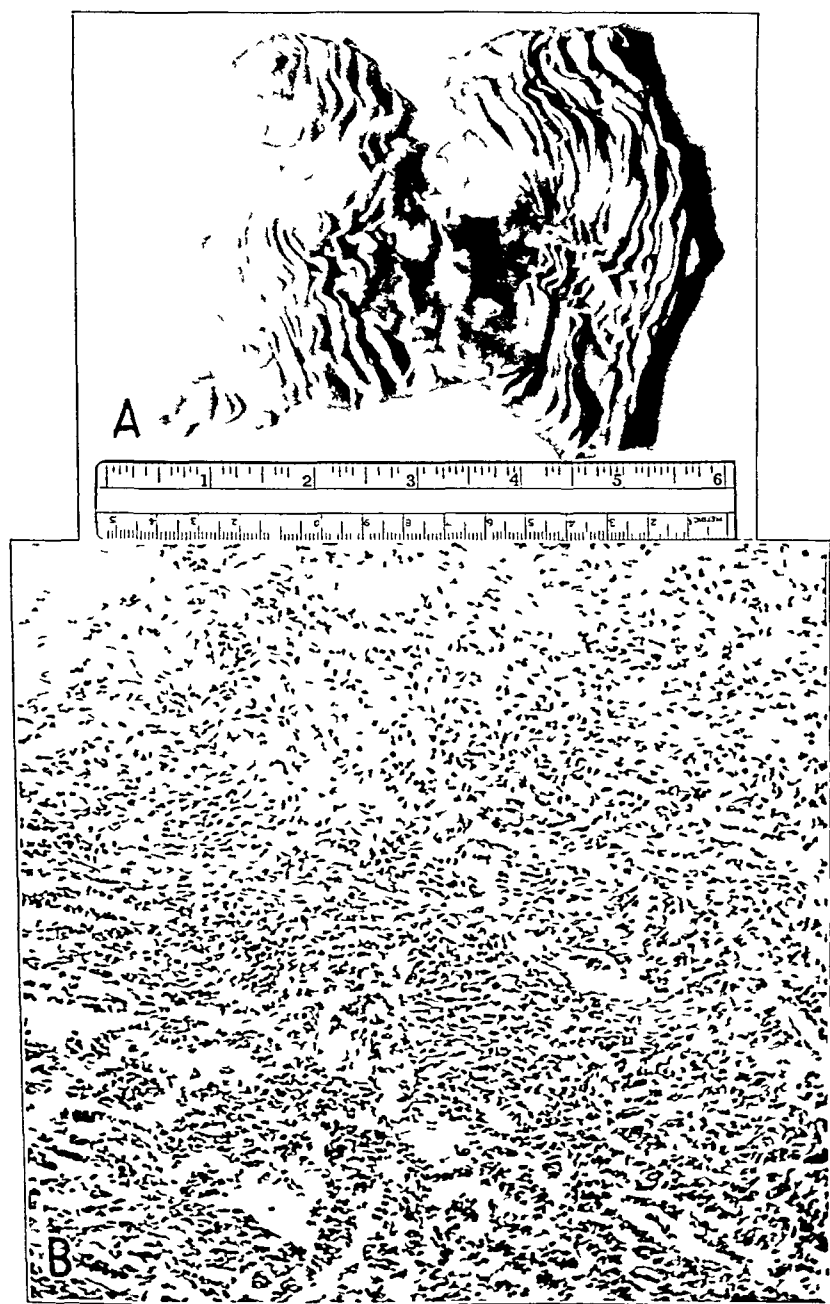


Fig 8—Carcinoma of the jejunum A mucosal surface, B, microscopic section

movements of distended loops of bowel. The leukocyte count was 9,400 per cubic millimeter, with the following differential count: band forms, 12 per cent, polymorphonuclears, 66 per cent, lymphocytes, 18 per cent, and monocytes, 4 per cent. The urine was normal.

The symptoms described by the patient, together with the physical findings and the negative roentgen reports on the large bowel suggested the diagnosis of an obstructive lesion of the small bowel, with an acute episode, possibly perforation, superimposed.

With the use of spinal anesthesia a right midrectus incision was made. When the peritoneal cavity was entered 2 liters of turbid fluid was encountered, which contained some barium. Particles of barium were also found covering the intestines. A tumor mass involving the jejunum was found with a perforation near its center. Numerous glands were found in the mesentery, but the liver and other viscera were not involved. A wide resection of the jejunum was made, and continuity was restored by a side to side anastomosis. A cigaret drain was placed in the pelvis.

The patient made an uneventful recovery from the operation and was discharged from the hospital on the fourteenth day after operation.

Pathologic Report—Gross Picture. The specimen was a resected portion of small intestine, measuring 14 by 9 cm. It was open. In approximately the center of the bowel was an ulcerated mass measuring 6 cm in diameter. The edges were raised, nodular and thickened. The floor was necrotic and hemorrhagic and exhibited near the center a 3 mm perforation which extended through all the coats to the serosa. The wall was markedly thickened and indurated about the region of the ulcer. The overlying serosa was infiltrated and edematous. The remainder of the intestine showed no gross pathologic change. Several minute lymph nodes were found close to the mesenteric attachment.

Histologic Picture. The general microscopic picture and character of the mural infiltration suggested anaplastic carcinoma rather than sarcoma. The growth was probably one of the rare primary tumors of the small intestine. The diagnosis was anaplastic carcinoma.

Follow-Up.—In this case the patient shows no recurrence of symptoms at present.

SUMMARY

The types, clinical aspects and treatment of benign and malignant tumors of the small intestine are discussed. Seven cases are reported.

Dr. Joseph Felsen, Director of Laboratories and Research at the Bronx Hospital, permitted the use of the photographs, photomicrographs and pathological reports.

PARTIAL AGENESIS OF THE CORPUS CALLOSUM

DIAGNOSIS BY VENTRICULOGRAPHIC EXAMINATION

ALONZO B. CASS, M.D.

AND

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LOS ANGELES

Although Reil¹ described the first case of agenesis of the corpus callosum as early as 1812 the apparent rarity of the condition is indicated by the fact that Baker and Graves,² reviewing the literature in 1933, discovered only 81 reported cases to which they added 1 of their own. Of the 82 cases, only 2 were reported in the United States. Archambault³ in 1911 described a case of complete agenesis. In the case reported by Baker and Graves the agenesis was partial.

Until the introduction of ventriculography in 1918⁴ and encephalography in 1919⁵ by Dandy there was no method of diagnosing the condition during life and for this reason agenesis of the corpus callosum was invariably discovered unexpectedly at autopsy.

Apparently Guttmann⁶ made the first encephalographic study of this condition in 1929. His description of the encephalographic picture was typically that of agenesis of the corpus callosum, but the characteristic changes in the encephalogram were not recognized and the diagnosis was not made during the life of the patient. The anomaly was discovered accidentally at postmortem examination.

The first published report of the diagnosis of agenesis of the corpus callosum by encephalographic methods was made by Davidoff and

From the Children's Hospital

1 Reil J. Mangel des mittleren und freien Theils des Balkens in Menschenhirnen. *Arch f d Physiol* **11** 341 1812

2 Baker R and Graves G. Partial Agenesis of the Corpus Callosum. *Arch Neurol & Psychiat* **29** 1054 (May) 1933

3 Archambault LaSalle. A Contribution to the Anatomy and Pathology of Agenesis of the Corpus Callosum. *Albany M Ann* **32** 513, 1911

4 Dandy W E. Ventriculography. *Ann Surg* **68** 5 1918

5 Dandy W E. Roentgenography of the Brain After the Injection of Air in the Spinal Canal. *Ann Surg* **70** 397 1919

6 Guttmann L. Ueber einen Fall von Entwicklungsstörung des Gross- und Kleinhirns mit Balkenmangel. *Psychiat neurol Wechnchr* **31** 453 1929

Dyke⁷ in a paper read before the American Association of Neuro-pathologists Dec 28, 1933 Hyndman and Penfield⁸ reported 2 cases at the sixtieth annual meeting of the American Neurological Association, in June 1934, and added 3 more in an article published June 1937

Interestingly, in each of these reports the clinical diagnosis in the first cases was cyst of the septum pellucidum The first patient of Dyke and Davidoff⁷ was a white girl aged 6 years An encephalogram taken Dec 11, 1930 was typical of agenesis of the corpus callosum, but the diagnosis was not made until autopsy, death having followed a small osteoplastic craniotomy on the right side, performed on Oct 24, 1933 for a supposed cyst of the cavum of the septum pellucidum At the time the encephalogram was taken, the large collection of air seen between the lateral ventricles, which included the space normally occupied by the third ventricle, was interpreted as filling the cavity of the septum pellucidum and the cavum Vergae, the walls of which were ruptured during the procedure, allowing the escape of fluid and permitting filling with air Moreover, the diminution of epileptic seizures during the subsequent two years seemed to verify the assumption that the cyst had ruptured during the insufflation with air

An encephalogram was taken of their third patient prior to verification of the lesion of the first patient, and again operation was undertaken on the basis of a mistaken roentgen diagnosis of cyst of the cavum septi pellucidi After the postmortem examination of the first patient of course the diagnosis of agenesis of the corpus callosum in the case of the third patient became evident

Similarly, the picture in the first case reported by Hyndman and Penfield⁸ "indicated an abnormal condition in the midline, and led us at first to suspect a cyst of the cavum septi pellucidi" It was for this reason that the patient, a child, was operated on, the possibility of partial agenesis of the corpus callosum was not considered

Because of a similar ventricular abnormality in their second case a small osteoplastic flap was turned over the longitudinal fissure When the right hemisphere was retracted from the falx, the unexpected condition was revealed Instead of the corpus callosum, only a translucent membrane bridged the bottom of the fissure The corpus callosum and the septum pellucidum seemed to be completely absent, but no other gross abnormality, except lateral displacement of the basal ganglia of each side and obvious enlargement of the ventricular system, was observed

7 Davidoff, L. M. and Dyke, C. G. Agenesis of the Corpus Callosum. Diagnosis by Encephalography, Report of Three Cases, *Am J Roentgenol* 32: 1934

8 Hyndman, O. R., and Penfield, W. Agenesis of the Corpus Callosum. Its Recognition by Ventriculography, *Arch Neurol & Psychiat* 37: 12, 1937

As a result of these findings and in view of the characteristic encephalographic picture, the condition in their 3 subsequent cases was immediately recognized

Prior to this time, attention had been called to congenital cerebral cysts of the cavum septi pellucidi and the cavum Vergae in Dandy's interesting paper,⁹ but the differences in the pneumographic features of these cysts and agenesis of the corpus callosum had not yet been appreciated

Since the collection of 82 cases by Baker and Graves,² 17 additional cases have been reported These include the 3 cases of Davidoff and Dyke and the 5 of Hyndman and Penfield In 1 other, mentioned by Hyndman and Penfield⁸ and included by Dandy¹⁰ in Dean Lewis' "Practice of Surgery," the ventriculogram showed a congenital deformity of the brain which was without doubt agenesis of the corpus callosum The other cases are those reported by de Morsier and Mozer,¹¹ and the 6 reported by Juba,¹² Regier¹³ and Segal¹⁴ (2 by each author)

To these we add our present case, which brings the total of those reported to 100 Ours is the ninth instance of this anomaly in which the condition was diagnosed during the patient's life by cerebral pneumographic examination and the diagnosis was made at the earliest age on record

EMBRYOLOGY

Retzius has demonstrated the corpus callosum as an outgrowth of the lamina terminalis Its formation occurs during the third and fourth months of fetal life, progresses concomitantly with the development of the hippocampal commissure and the septum pellucidum and becomes complete by the fifth month¹⁵

9 Dandy, W E Congenital Cerebral Cysts of the Cavum Septi Pellucidi (Fifth Ventricle) and Cavum Vergae (Sixth Ventricle), *Arch Neurol & Psychiat* **25** 44 (Jan) 1931

10 Dandy, W E, in Lewis, D Practice of Surgery, Hagerstown, Md, W F Prior Company, Inc, 1930 vol 12, p 331

11 de Morsier, G, and Mozer, J I Agénésie complète de la commissure calleuse et troubles du développement de l'hémisphère gauche avec hémiparésie droite et intégrité mentale (Le syndrome embryonnaire précoce de l'artère cérébrale antérieure), *Schweiz Arch f Neurol u Psychiat* **35** 64 and 317, 1935

12 Juba, A Ueber einen mit Cystenbildung des Gehirns, Heterotopie der Plexus Chorioidei und Mikrogylie verbundenen Fall von vollständigem Balkenmangel *Arch f Psychiat* **102** 731, 1934, Ueber vollständigen Balkenmangel bei einem 39 jährigen geistig normalen Menschen, *Ztschr f d ges Neurol u Psychiat* **156** 45 1936

13 Regier, A Ueber zwei Fälle von Balkenlosigkeit am menschlichen Gehirn *Schweiz Arch f Neurol u Psychiat* **36** 306, 1935, **37** 99, 1936

14 Segal, M Agenesis of the Corpus Callosum in Man, *South African J M Sc* **1** 65 1935

15 Keibel, F, and Mall, F Manual of Human Embryology Philadelphia, I B Lippincott Company 1912, vol 2, pp 91 95

As is shown so well by the diagrams of Hyndman and Penfield,⁸ the anlage of the corpus callosum becomes visible during the third month of intrauterine life as a cephalic projection from the lamina terminalis. As this anterior aspect of the corpus callosum develops, it progresses posteriorly over the fimbria and the thalamus. In its posterior progress it carries the septum pellucidum beneath it. This triangular structure subsequently becomes bounded by the corpus callosum anteriorly and superiorly, the hippocampal commissure of the crura of the fornix posteriorly and the lamina rostralis inferiorly.

From such embryonic development, it is obvious that associated structures may well be affected by agenesis of the corpus callosum.

The development of the corpus callosum in higher mammals has led to a zoologic division of this highest class of vertebrates into two subclasses, the callosal and the acallosal mammals. The structure reaches its highest degree of development in the primates and becomes little more than a membranous structure in the lowest group of callosal mammals. As has been pointed out by Cameron,¹⁶ the formation of convolutions in the brain increases its total volume three times, and the size of the corpus callosum is always proportional to this volume.

As might have been expected, absence of the corpus callosum in animals has been reported. King and Keeler¹⁷ discovered agenesis of the corpus callosum in a strain of house mice, many of which showed abnormal absence of the rods in the retina. These authors found that the agenesis was familial and was probably inherited as a unit character. In the animals studied by them the corpus callosum was either present or entirely absent. A superficial examination of the reactions of the mice with and those without a corpus callosum revealed nothing distinguishing. Tumbelaka¹⁸ has described total agenesis of the corpus callosum in a cebus monkey.

AGE INCIDENCE

In the majority of cases this condition has been disclosed at autopsy in persons less than 10 years old. Hayek¹⁹ reported partial agenesis

16 Cameron, J. L. The Corpus Callosum. A Morphological and Clinical Study, *Canad. M. A. J.* 7: 609, 1917.

17 King, L. S., and Keeler, C. E. Absence of the Corpus Callosum. Hereditary Brain Anomaly of the House Mouse, Preliminary Report. *Proc. Acad. Sci.* 18: 525, 1932. King, L. S. Absence of the Corpus Callosum. Hereditary Defects of the Corpus Callosum in the Mouse, *Mus. Musculus*, *J. Comp. Neurol.* 64: 337, 1936.

18 Tumbelaka, R. Das Gehirn eines Affen worin die interhemisphärische Balkenverbindung fehlte, *Folia neurobiol.* 9: 1, 1935.

19 Hayek, H. Ueber einen Fall von Hypoplasie des Balkens in einem gehärteten Gehirn eines Neugeborenen, *Virchows Arch. path. anat.* 273: 1, 1929.

a newborn infant, de Crinis²⁰ complete agenesis in an infant 2 weeks old and de Lange²¹ complete agenesis in a baby aged 5 months who had died of pneumonia. The anomaly has been found at almost all ages the upper limit being represented by 2 patients who died respectively, at the ages of 72²² and 73 years²³

CAUSES OF AGENESIS OF THE CORPUS CALLOSUM

The causes suggested for developmental peculiarities in general have been advocated in cases of this anomaly. In Banchi's case²³ absence of the corpus callosum was unassociated with other important anomalies. For this reason he claimed that the condition was the result of a circumscribed pathologic process in the mesial side of the embryonic lamina terminalis. Such a simple explanation is, of course untenable in other cases, for so many anomalies are present that the entire brain must be considered pathologic.

Stoecker's patient²⁴ died of juvenile dementia paralytica (syphilis was probably the cause) and Landsbergen²⁵ expressed the belief that the presence of hereditary syphilis was probable in his case.

Several authors have explained the origin on the basis of the rather constantly present hydrocephalus which enlarges the distance between the hemispheres and prevents the crossing. They have interpreted the hydrocephalus on the basis of ependymitis and when this condition could not be found they assumed that it had been present formerly.

De Lange²¹ pointed out that if hydrocephalus is not already present during the third month of fetal life it cannot account for the absence of the corpus callosum and she proposed a lesion of the germ as the cause.

Because the corpus callosum normally forms the roof of the lateral ventricles, Cameron¹⁶ stated that the hydrocephalus is more apparent than real.

At all events it seems hardly possible that hydrocephalus can precede the formation of the corpus callosum.

20 de Crinis M. Ueber einen Fall von Balkenmangel. *J f Psychol u Neurol* **37** 443, 1928.

21 de Lange, C. On Brains with Total and Partial Lack of the Corpus Callosum and on the Nature of the Longitudinal Callosal Bundle, *J Nerv & Ment Dis* **62** 449 1925.

22 Poterin Dumontel. Absence congenitale du corps calleux sans troubles fonctionnels durant la vie. *Compt rend Soc de biol* **4** 94, 1863. *Gaz d hop* **36** 47 1863.

23 Banchi A. Studio anatomico di un cervello senza corpo calloso, *Arch ital di anat e di embriol* **3** 658 1904.

24 Stoecker W. Ueber Balkenmangel im menschlichen Gehirn. *Arch f Psychiat* **50** 543 1912.

25 Landsbergen F. Ueber Balkenmangel. *Ztschr f d ges Neurol u Psychiat* **11** 515 1912.

Chemical toxins have been proposed as an etiologic factor, but there is no substantial evidence of their influence.

Whatever the cause in any particular case may be, it seems obvious that this anomaly is due to arrest of the normal development of the callosal body, which of course may occur at any stage.

ANOMALIES ASSOCIATED WITH AGENESIS OF THE CORPUS CALLOSUM

Certain anomalies of the brain are almost constantly associated with absence of the corpus callosum. Dilatation of the posterior horns of the lateral ventricles is most frequently encountered. With this dilatation occurs a thinning of the walls of the posterior horns. The calcarine and parieto-occipital sulci are prevented from joining by the interposition of a superficial gyrus.

On the mesial aspect of the cerebral hemisphere the sulci possess a radiating arrangement. Prior to the formation of the corpus callosum, similar shallow sulci, radially arranged, are frequently visible on the mesial aspects of the embryonic cerebral hemispheres. These are felt to be natural, though transitory, structures. For this reason it would seem that the radial arrangement of the convolutions and sulci of the mesial aspect of the brain in cases of agenesis of the corpus callosum represents a similar preservation of this primitive transitory arrangement occurring prior to the third month of fetal life, before the formation of the corpus callosum. This probability is supported not only by the fact that the radial arrangement of the convolutions and sulci is preserved in cases of complete agenesis of the corpus callosum but by the observation that when partial agenesis exists such radial arrangement is absent dorsal to the partially formed corpus callosum and is again preserved where the latter structure has failed to develop.

In most cases the condition is associated with some other anomaly, such as microcephaly, porencephaly, polygyria, absence of the olfactory nerves, incomplete separation of the frontal lobes, hydrocephalus, or an enlarged anterior commissure.

In the study of her case, Lange²¹ found inhibition in development of the cortex revealed by the presence of the internal granular area throughout in the brain. Moreover, the granularis interna in the area of the calcarine fissure was not divided into the three layers. According to Brodmann,²⁶ this separation occurs normally in a 7 month fetus.

Lipoma associated with agenesis of the corpus callosum has been reported on numerous occasions. Huebschmann²⁷ described an instance

²⁶ Brodmann, K. *Vergleichende Lokalisationslehre der Grosshirnrinde*, J. A. Barth, 1909.

²⁷ Huebschmann. *Ueber einige seltene Hirntumoren*, III. I. 1921, bei partiellem Balkenmangel, *Deutsche Zeitschrift für Nervenheilkunde* 72: 222.

of partial absence in which a lipoma was situated on the genu of the corpus callosum, and Huddleson,²⁸ a case in which a lipoma was situated between the frontal lobes

Bodily defects accompanying agenesis of the corpus callosum have only occasionally been reported. These have included cleft palate and harelip, heteropia of the brain substance, cryptorchidism and malposition of the stomach high in the thorax. Physical development is often above the average in patients with absence of the corpus callosum.

Complete agenesis of the corpus callosum has been observed in more than half the cases. The analysis of Mingazzini²⁹ revealed that of 71 cases complete agenesis was present in 43 and partial agenesis in 28.

Forms of partial agenesis of the corpus callosum may vary from one in which the structure is complete except for a defective splenium to one in which there is only a rudimentary bundle of fibers in the region of the genu, with consequent absence of the septum pellucidum.

On the basis of the embryonic period in which arrest occurs, Bruce³⁰ divided defects of the corpus callosum into four main types. When the development continues until the end of the fourth month the genu and the posterior extension of the corpus callosum will be present. If development ends at the fourth month the anterior commissure will be formed by union of the laminae of the septum pellucidum at their anterior inferior angles. When arrest occurs prior to the fourth month the corpus callosum, septum pellucidum, lyra of the fornix and anterior commissure will be absent, but the hemispheres will be divided. If arrest begins during the first three weeks of embryonic life not only will the corpus callosum, septum pellucidum, fornix, velum interpositum and anterior commissure be absent, but the cerebrum will consist of a single vesicle and the ventricle of a single cavity.

FUNCTION OF THE CORPUS CALLOSUM

As a result of their experimental work on monkeys, Lafora and Prados³¹ found that depending on whether the location is anterior or posterior, section of the corpus callosum was followed by paralysis of the upper or of the lower extremities. Moreover, they discovered that section on either the right or the left side was followed by a series of phenomena identical with those of crossed hemiplegia.

28 Huddleson J. H. Ein Fall von Balkenmangel mit Lipomentwicklung im Defekt. *Ztschr f d ges Neurol u Psychiat* **113** 177 1928.

29 Mingazzini G. Der Balken. Eine anatomische physio-pathologische und klinische Studie, Berlin Julius Springer, 1922.

30 Bruce A. On the Absence of the Corpus Callosum in the Human Brain with the Description of a New Case. *Brain* **12** 171 1889.

31 Latorre G. R. and Prados A. Such M. Investigaciones experimentales sobre la function del cuerpo calloso. *Siglo med* **69** 169, 1922.

Later work by Seletzky and Gilula³² on dogs and rabbits revealed that section of the hindpart of the corpus callosum caused little disturbance, except slight ataxia of the extremities. Section of the anterior or the middle part of the corpus callosum resulted in a disturbance of sensibility, sometimes in all the extremities, sometimes in only some and sometimes in the body or trunk. The gait became ataxic. Disturbance of the sense organs on the side of the section occurred, resulting in loss of hearing, sight or the sense of smell. Occasionally the animals tended to move in circles. Interestingly, all of the symptoms previously described disappeared after a variable interval, and no further abnormalities were observed. This important fact has been overlooked by many authors.

According to Mingazzini,²⁹ one differentiates internal, mesial and inferior fibers in the corpus callosum. The internal fibers come from the gyrus fornicatus, the internal superior surface of the gyrus frontalis, the upper third of the rolandic convolution and the paracentral and superior parietal gyri. The mesial fibers arise from the external superior surface of the cerebral hemisphere, chiefly from the lower portions of the frontal lobes and partly from the middle third of the rolandic convolution and inferior parietal lobule. For this reason he suggested that a section through the internal and mesial layers might produce a disturbance in gait (interruption of the fibers from the frontal and parietal convolutions) together with psychic alterations, such as apathy and diminished motility.

The fibers of the lower layer come from the gyrus operculi, as well as from the posterior portions of the first and second temporal convolutions and from the island of Reil. On this basis Mingazzini explained the disturbance in taste and hearing.

As early as 1885, Hamilton³³ demonstrated that after crossing in the corpus callosum some of the fibers end in identical and distant areas of the cortex while others are lost in the thalamus and in the internal and external capsules.

Mingazzini²⁹ showed that some of the callosal fibers originate from the pyramidal cells in the cortex.

Mott and Schaefer³⁴ were able to demonstrate the presence of motor projection pathways in the corpus callosum by electrical stimulation. Stimulation of the genu apparently provoked movements of the head and neck, and as stimuli approached the splenium the motor response progressed caudad. The splenium seemed to be devoid of motor components.

32 Seletzky, W., and Gilula, J. Zur Frage der Funktionen des Corpus Callosum bei Tieren, *Arch f Psychiat* **86** 57, 1928.

33 Hamilton, D. On the Corpus Callosum in the Adult Human Brain, *Philos Trans R Soc Lond* & *Physiol* **19** 385, 1885.

34 Mott, F., and Schaefer, E. On Movements Resulting from Electrical Stimulation of the Corpus Callosum in Monkeys, *Brain* **13** 174, 1890.

Study of a series of 5 cases of tumor of the corpus callosum by Alpers and Grant³⁵ indicated that the outstanding symptoms were inability to concentrate and maintain attention, motor signs, such as hemiparesis or weakness of all extremities and apraxia. It is important to observe however that the same symptoms are not present in cases of agenesis.

In this regard, as was emphasized by Armitage and Meagher³⁶ positive deductions from the study of patients presenting gross lesions of the corpus callosum may be easily misleading because of the inevitable involvement of neighboring structures. This was particularly true in cases of tumor of the brain. After an extensive study of cases in Cushing's clinic, they could assign no function to the corpus callosum. Moreover, they were unable to detect any apraxia in patients after partial section of the corpus callosum in the midline and found no evidence of disturbance in motor or mental reactions in *Macacus rhesus* monkeys after complete transection of the commissure.

In 1921, Cameron and Nicholls³⁷ came to the following conclusion concerning the mental status of patients with agenesis of the corpus callosum:

Such meagre evidence as we possess seems to indicate that the callosal fibers are of more importance in maintaining and governing the finer co-ordinations of muscular movement in the limbs of the opposite sides than in regulating the higher functions of mentality.

As a result of their work, Kennard and Watts³⁸ concluded that section of the corpus callosum in monkeys produced no motor weakness and did not cause forced grasping but did give rise to a definite syndrome characterized by inertia and slowness in initiating purposeful movements. Moreover, section of the corpus callosum subsequent to unilateral lesions of the motor areas produced no additional motor deficit in the contralateral extremities.

These authors found further that a unilateral lesion of the motor or premotor areas subsequent to section of the corpus callosum was followed by no greater deficit than that seen with the same lesion when the corpus callosum was intact. Ipsilateral movement from stimulation of area 6 was not abolished by section of the corpus callosum.

³⁵ Alpers, B. J. and Grant, F. C. The Clinical Syndrome of the Corpus Callosum, *Arch. Neurol. & Psychiat.* **25**: 67 (Jan.) 1931.

³⁶ Armitage, G. and Meagher, R. Gliomas of the Corpus Callosum, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **146**: 454, 1933.

³⁷ Cameron, J. L. and Nicholls, A. Two Rare Abnormalities Occurring in the Same Subject. Partial Absence of the Corpus Callosum, the Stomach Situated Entirely Within the Thorax, *Canad. M. A. J.* **11**: 448, 1921.

³⁸ Kennard, M. A. and Watts, J. W. Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys. *J. Nerv. & Ment. Dis.* **79**: 159, 1934.

Prior to the introduction of encephalographic diagnosis it was necessary, of course, for the physician to study the patient's mental activity and behavior in retrospect after the postmortem examination had revealed the diagnosis. In this way, in a number of cases, notably those collected by Bruce,³⁹ a normal condition was reported. From a study of 15 cases reported in the literature and 1 of his own, Bruce concluded that if the brain is otherwise well developed, absence of the corpus callosum does not necessarily produce any disturbance of motility, coordination, general or specific sensibility, reflexes, speech or intelligence.

Cameron stated the opinion⁴⁰ that total absence of the corpus callosum is possible without any pathognomonic alteration in the subject's mental or physical capacity.

Dandy³⁹ divided the corpus callosum in its entire anteroposterior extent and noted no unusual results.

Hartman and Trendelenburg⁴⁰ taught both rhesus and Javanese monkeys to perform a complicated series of bimanual movements necessitating the simultaneous use of the two hands in obtaining food. After total section of the corpus callosum these animals showed no evidence of apraxia.

The experiments of Pavlov⁴¹ disclosed that when a reflex, such as the tactile salivary reflex, is conditioned on one side of the body, stimuli applied to corresponding locations on the opposite side of the body produce the same reflex. Division of the corpus callosum by operation abolished the phenomenon entirely, in other words, it is necessary to condition the reflex on the two sides of the body independently.

CLINICAL MANIFESTATIONS

Impaired mentality and epilepsy are the most frequent clinical manifestations associated with agenesis of the corpus callosum. The intellectual status of the patients varies from idiocy to mediocrity. Patients living to an advanced age are, as a rule, of mediocre intelligence. The epileptic seizures may be of the petit mal or of the grand mal type.

The history of a patient with agenesis seldom suggests the function of the corpus callosum, for other anomalies of the brain so becloud the picture that little remains which might be explained by its presence.

39 Dandy, W. E. Operative Experience in Cases of Pineal Tumor. *Arch Surg* **33** 19 (July) 1936.

40 Hartman, F., Jr., and Trendelenburg, W. Zur Frage der Bewegungsstörungen nach Balkendurchtrennung an der Katze und am Affen, *Ztschr. f. exper. Med* **54** 578, 1927.

41 Pavlov, I. Conditioned Reflexes. An Investigation of the Physiological Activity of the Cerebral Cortex, translated and edited by G. Anrep. London: University Press, 1926.

In addition to epilepsy and feeble-mindedness, spastic paraplegia, nystagmoid movements of the eyes and continued movement of the hands have been reported. As Cameron and others have emphasized, however, defects other than those of the corpus callosum account for the epilepsy and spastic paraplegia in such cases.

All the 3 patients in the cases reported by Davidoff and Dyke⁷ suffered from epileptic seizures, and the third patient, a child aged 3 years, was also retarded in mental and physical development. Until she was 19 months old she was unable to walk, and at the age of 3 years she was able to speak only a few words. Their first patient, a child aged 6 years, showed a high average intelligence quotient on the Merrill-Palmer scale.

Of the 5 patients whose cases were reported by Hyndman and Penfield,⁸ 4 were epileptic. The patient without epileptic seizures, a boy aged 2 years, was retarded. Not only was he unable to sit up, but he took little or no interest in his surroundings.

In spite of the infrequency of agenesis of the corpus callosum as recorded in the literature, the anomaly probably occurs more often than is thus suggested. This is corroborated by the fact that 3 cases were discovered by Davidoff and Dyke⁷ from the 1,100 encephalograms taken during a three year period at the Neurological Institute of New York.

As the use of encephalographic procedures in the study of epileptic and mentally defective persons becomes more frequent, many more cases will be recognized.

REPORT OF A CASE

M. F., a boy aged 9 months, was admitted to the Children's Hospital on Jan. 25, 1938, because of retarded development. Delivery had occurred normally at full term. After birth there was no difficulty with the feedings, but later the child did not seem to progress normally. His parents observed that he was 6 months old before he could hold up his head and about 8 months old before he began to play with toys or made any effort to grab at objects. Recently, although the baby had eaten well, he had failed to gain in weight. At the time of examination, at 9 months, he made no attempt to sit up and was unable to roll over by himself.

Examination—The child's head was not noticeably high and broad from side to side, the occiput was flat and the frontal bosses prominent (fig. 1A). The anterior fontanel was patent, admitting about one finger tip, but did not indicate increased pressure. The superficial veins over the scalp were somewhat dilated. Examination otherwise disclosed nothing noteworthy except oscillating nystagmus on lateral and upward gaze and the fact that the baby could not sit up and took little interest in his surroundings.

Urinalysis gave normal results. The hemoglobin content of the blood was 75 per cent. There were 4,390,000 erythrocytes and 8,350 leukocytes per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenograms of the long bones taken during the last three months as reported by Dr. Rolla G. Kirschner showed osseous development typical of that of a child aged 4 years.



Fig 1—Photographs of M F at the age of 1 year, taken three months after ventriculographic examination A, lateral view, showing the flatness of the occiput and prominence of the frontal bosses B, anterior view

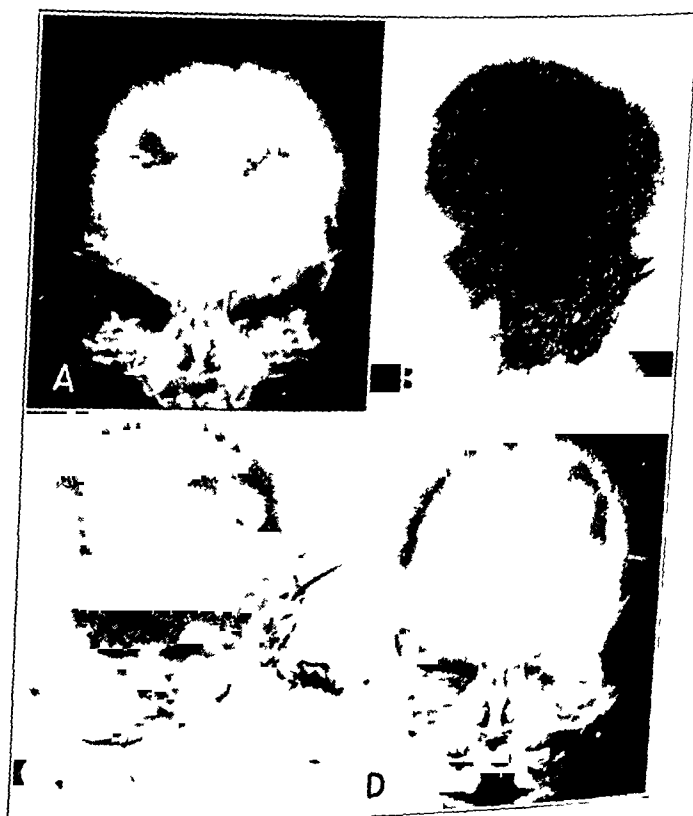


Fig 2—A, anteroposterior ventriculogram (brow up) showing partial atrophy of the corpus callosum The hydrocephalus is evident, and the normally closely apposed but widely separated lateral ventricles are shown The third ventricle is clearly seen, but its vertical extent is increased B, lateral ventriculogram (occiput up) The dilatation of the posterior horns of the lateral ventricle is demonstrated C, lateral ventriculogram (right side up) The third ventricle appears to extend abnormally high and has a "cocked hat" appearance D, posteroanterior ventriculogram (brow up) The wide separation of the posterior horns of the lateral ventricle is evident

The impression after examination at this time was that the patient had hydrocephalus of the communicating type, and pneumographic studies were recommended. The baby had a cold and fever and was sent home until these conditions should subside.

Because of the possibility of increased intracranial pressure and adhesions in the region of the basal cistern, the ventriculographic procedure was felt to be preferable to the encephalographic. The former was carried out, accordingly, on the infant's return to the hospital on February 4.

Approximately 10 cc of ventricular fluid was withdrawn and 10 cc of air injected. Roentgenograms were then taken, which revealed a picture which we felt was consistent with a diagnosis of partial agenesis of the corpus callosum.

The filling was fairly adequate. The anteroposterior view disclosed definite hydrocephalus, with normally shaped anterior horns, which, however, were wide apart. The greatest separation of the lateral ventricles was 4.5 cm. The mesial margin of the right ventricle was slightly concave, but not that of the left. Although in this view the third ventricle was not distinct, its vertical extent was 3.5 cm and its width 0.6 cm (fig 2 A).

The lateral view, taken with the occiput up, revealed particularly well the marked dilatation of the posterior horns so consistently found in cases of agenesis of the corpus callosum (fig 2 B). The other lateral views also demonstrated this dilatation, but the third ventricle was shown well in only one roentgenogram, in which the abnormal height and "cocked hat" appearance, spoken of by Davidoff and Dyke, seemed to be present (fig 2 C).

The posteroanterior view revealed well the marked separation of the posterior horns of the lateral ventricles (fig 2 D).

DIFFERENTIAL DIAGNOSIS

Cyst of the septum pellucidum, or the so-called fifth ventricle as described by Dandy,⁹ is the one condition likely to be confused with the pneumographic picture of agenesis of the corpus callosum. This is borne out by the fact that in the first cases in the series reported by Davidoff and Dyke and by Hyndman and Penfield the patients were operated on for supposed cysts of the septum pellucidum.

Interestingly, the clinical features of cases of cysts of the septum pellucidum are not unlike those found in cases of agenesis of the corpus callosum. The patients in the 5 cases reported by Verga,⁴² in which this cavity was discovered at necropsy, were from psychopathic wards and showed varying degrees of mental disturbance. Another such anomaly demonstrated to Verga by his friend Sangalli as cited by Dandy⁹ occurred in a 17 year old girl with epilepsy.

The patients in the cases reported by Gibson⁴³ and Thompson⁴⁴ were psychopathic. In addition Thompson's patient was judged to be an imbecile.

⁴² Verga, A. Dell' apparato ventricolare del setto lucido e della volta a tre pilastri, *Gior r Ist lomb di sc*, 1855 nos 43 and 44 p 89. Sul ventricolo della volta a tre pilastri. *Gazz med ital lomb* 2 225 1851.

⁴³ Gibson, J K. A Perforated Septum Pellucidum. *Anat Rec*, 28 103, 1924.

⁴⁴ Thompson I M. On Certain Abnormal Conditions of the Septum Pellucidum. *Univ California Publ, Anat* 1 21 1932.

One of Dandy's⁸ patients, a boy aged $4\frac{1}{2}$ years, had a history of retarded development, was mentally backward and suffered from peculiar epileptic attacks, of varying character

A space-occupying cyst between the lateral ventricles often causes symmetric separation of the anterior horns and bodies of the lateral ventricles, but usually produces mesial excavation as well as separation of the anterior horns. However, unless the cyst communicates with the ventricular system it will not be visualized with air. The characteristic picture of the third ventricle in cases of agenesis of the corpus callosum, then, further establishes the differential diagnosis

As has been pointed out by Dandy,⁹ most cysts of the septum pellucidum which are of unusual size have been observed at necropsy to communicate with the ventricular system by one or more openings into the third and lateral ventricles

Because of their inconstant position, size and number, and particularly because their borders are ragged and uneven, it is evident that these openings are not preformed, as are the interventricular foramina

Thompson⁴⁴ reviewed the literature on the subject and included the cases of communicating cava

In cases of communicating cysts of the septum pellucidum, it is possible that ventriculographic examination would reveal a picture similar to that of agenesis of the corpus callosum. The lateral ventricles would be symmetrically separated. A large body of air symmetrically placed and reaching higher than the normal extension of the third ventricle would be shown

Hyndman and Penfield⁸ pointed out that except for a bicornuate appearance of the lateral ventricles, a communicating, enlarged cavum septi pellucidi might well present a picture identical with that of agenesis of the corpus callosum. They concluded, therefore, that the bicornuate appearance of the lateral ventricles is the pathognomonic indication of agenesis of the corpus callosum

As was emphasized by Davidoff and Dyke,⁷ the cardinal encephalographic changes in cases of agenesis of the corpus callosum are (1) marked separation of the lateral ventricles, (2) angular dorsal margin of the lateral ventricles, (3) concave mesial borders of the lateral ventricles, (4) dilatation of the posterior horns of the lateral ventricle, (5) elongation of the interventricular foramina, (6) upward extension and dilatation of the third ventricle, with a "cocked hat" appearance, and (7) radial arrangement of the mesial cerebral sulci around the third ventricle and their extension through the zone occupied by the corpus callosum

Although a ventricular picture of a communicating cyst of the septum pellucidum might closely simulate that of agenesis of the corpus callosum

it would without doubt show sufficient variation from the cardinal changes just described to allow a reasonably accurate differential diagnosis to be made

We feel that the case here reported is one of partial agenesis of the corpus callosum. The lateral ventricles, though abnormally separated, do not, of course, present the upside-down, bicornuate appearance of the lateral ventricles pathognomonic of pronounced agenesis of the corpus callosum. The posterior horns of the lateral ventricles were markedly dilated and separated, and in one view the third ventricle appeared to extend upward and to have the "corset-shaped" or "cocked hat" appearance so often associated with agenesis of the corpus callosum.

Though we believe it to be unlikely, a communicating cyst of the septum pellucidum cannot be entirely excluded in this case.

This infant will be followed with considerable interest. If possible, encephalograms will be taken at later stages of his life. Should death occur and necropsy be performed the certain diagnosis of the congenital anomaly will be established.

SUMMARY

A case presumed to be an instance of partial agenesis of the corpus callosum in a 9 month old infant is reported.

This is the ninth case in which this anomaly has been diagnosed during life by cerebral pneumographic examination, and the diagnosis was made at the earliest age on record.

Roentgenograms of the long bones show development typical of that of a 4 year old child.

The baby shows the developmental retardation often observed in patients with agenesis of the corpus callosum.

Eighteen cases, including the one reported here, have been added to the 82 collected by Baker and Graves in 1933.

REMOVAL OF PROCAINE FROM THE CEREBRO SPINAL FLUID DURING ANESTHESIA

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The duration of spinal anesthesia as ordinarily managed is not affected by any measures undertaken after the anesthetic has once been placed in the subarachnoid space. Studies on the concentration of procaine in the cerebrospinal fluid of patients under spinal anesthesia¹ have shown that after an initial period during which mechanical distribution away from the site of injection takes place there is a gradual disappearance of the procaine from the cerebrospinal fluid. These findings suggested that it might be possible to terminate anesthesia more quickly by removing the procaine from the subarachnoid space.

Adult patients were anesthetized by the subarachnoid injection of 150 mg of procaine hydrochloride between the second and the third lumbar vertebra, 3.5 cc of cerebrospinal fluid being used as the solvent. In different patients at various intervals after the initial injection a needle was reinserted at the site of injection and another was inserted into the subarachnoid space three interspaces above. Fluid was allowed to run off freely, and the subarachnoid space was washed out with from three to five successive 10 cc portions of sterile physiologic solution of sodium chloride. The original fluid and the washings were collected

From the Crown Heights Hospital

1 Koster, H., Shapiro, A., and Leikensohn, A. Procaine Concentration Changes at Site of Injection in Subarachnoid Anesthesia. *Am J Surg* 33:24-29, 1936. Concentration of Procaine in the Cerebrospinal Fluid of the Human Being After Subarachnoid Injection, *Arch Surg* 37:603-608 (Oct) 1938. Koster, H., Shapiro, A., and Warshaw, R. Concentration of Procaine in the Cerebrospinal Fluid of the Human Being After Subarachnoid Injection. Second Paper, to be published.

2 Koster, H. Spinal Anesthesia, with Special Reference to Its Use in the Head, Neck and Thorax, *Am J Surg* 5:554-570, 1928.

and measured, and then procaine content was determined photometrically after precipitation with vanillin and potassium mercuric iodide³

In the case of 3 patients no washing was done and fluid was collected only at the site of injection

Since it had been noticed that pain at the site of the operative wound returns at about the same time that the patient regains voluntary motor power in the legs the time when the patients were just able to move their legs was determined by frequent trial and used as a reference point for the duration of anesthesia

Duration of Motor Paralysis After Removal of Procaine

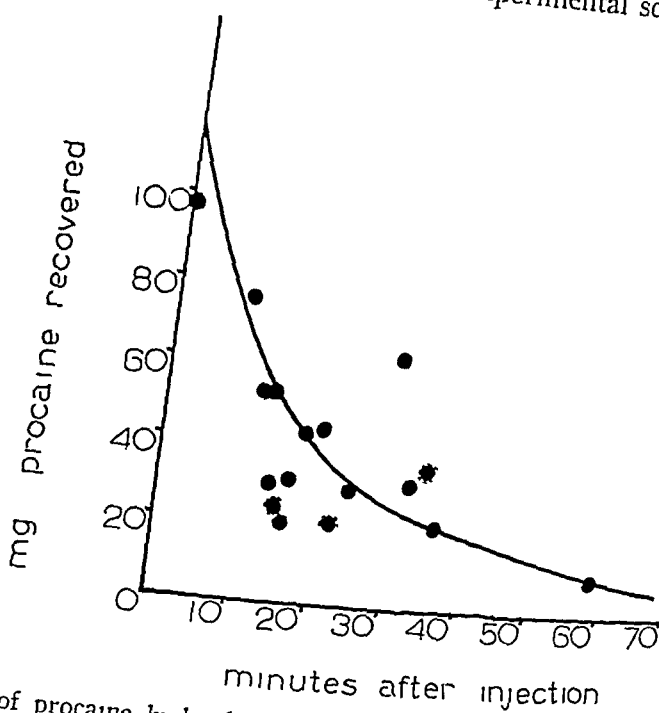
	Time from Injection to Washing Minute	Time from Washing to Recovery of Motor Power Minutes	Time from Injection to Recovery of Motor Power Minutes
With Washing			
1	0	0	0
2	9	9	18
3	12	15	27
4	14	11	25
5	16	5	21
6	16	1	29
7	17	12	29
8	18	12	30
9	20	9	29
10	20	4	24
11	30	3	33
12	36	4	40
13	59	2	61
Average	22	-	29
Without Washing			
1	13	13	26
2	22	23	45
3	31	24	55
Average	24	21	45

It has been observed¹ that motor power in the lower extremities returns about sixty minutes after the subarachnoid injection of 150 mg of procaine hydrochloride in 3.5 cc of cerebrospinal fluid. The duration of motor paralysis in patients studied in these experiments is shown in the accompanying table. For 13 patients in whose cases the washing of the subarachnoid space was begun at intervals up to fifty-nine minutes after the initial injection (average twenty-two minutes) the average duration of motor paralysis after the withdrawal of fluid was begun was seven minutes. The average total time from the initial injection to the end of motor paralysis was twenty-nine minutes.

³ Koster H, Shapiro A, and Posen E. A Micro Method for the Quantitative Determination of Procaine in Cerebrospinal Fluid. J Lab & Clin Med 21:1006-1008, 1936

In the 3 cases in which fluid was withdrawn but no washing was performed, the average time to the beginning of withdrawal was twenty four minutes and the average total duration of motor paralysis was forty-five minutes.

The chart shows the amounts of procaine hydrochloride recovered from the cerebrospinal fluid of different patients at various times after the initial injection. The three points in circles represent samples obtained by simple withdrawal without irrigation. They are included because when spinal fluid and washings were collected separately the procaine content of the washings was less than 10 per cent of the total procaine content of the washings was less than 10 per cent of the total a small error in comparison with the experimental scatter.



Amounts of procaine hydrochloride found in the spinal fluid and in washings obtained at various times after the subarachnoid injection of 150 mg of procaine dissolved in 3.5 cc of spinal fluid

Only 100 of the 150 mg of procaine injected could be recovered when the withdrawal and washing were begun at once. It is evident, therefore, that the ordinates in the chart represent amounts of procaine removable from the cerebrospinal fluid at various times and probably not the total amount of procaine remaining in the subarachnoid space. They must be corrected by a factor of +30 per cent in the early portions and perhaps more in the later portion in order to estimate the total amounts of procaine remaining in the subarachnoid space at various times after injection.

It is of interest also that the simple withdrawal of spinal fluid from a single needle yielded almost as much procaine as could be recovered

by irrigation with saline solution. Irrigation, however, was much more effective in terminating motor paralysis. This may have been due to the dilution of the remaining procaine by saline solution to a concentration below that necessary to maintain motor paralysis.

CONCLUSIONS

1 The duration of paralysis of the lower extremities in spinal anesthesia induced with procaine hydrochloride may be markedly shortened by withdrawing spinal fluid and irrigating the subarachnoid space with physiologic solution of sodium chloride between two needles.

2 When removal and washing are begun immediately after injection of the anesthetic, motor paralysis fails to develop.

3 The amount of procaine recoverable diminishes as the anesthesia progresses.

4 The maximum amount recovered when washing is begun immediately after injection of 150 mg of procaine hydrochloride is 100 mg.

5 Simple withdrawal is considerably less effective than irrigation in shortening the duration of motor paralysis, even though almost as much procaine is removed by the former method as by the latter.

WARM MOIST AIR THERAPY FOR BURNS

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AND

CHARLES BECK, MS

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The subject of wound healing of all types was thoroughly reviewed by Arey in 1936

Modern therapy for burns attempts to alleviate the subsequent toxemia and secondary shock of severe burns by rendering any supposed toxins arising from the heat-killed tissue insoluble. For many reasons, the conditions for healing under the coagulum of chemically coalesced debris do not approach the optimum conditions existing under the natural fibrin eschar (Carrel, Carrel and Baker¹)

The possibility of obtaining more rapid healing by providing a more nearly ideal physiologic environment for the wounded area led to the following study on rats, in which a comparative evaluation of various therapeutic agents and methods used as controls has been undertaken

METHOD

An experimental humidity chamber with a wood frame and glass windows, measuring 6 feet (180 cm) long, 3 feet (90 cm) wide and 3 feet (90 cm) high, with a displacement of 54 cubic feet (153 cubic meters), was built. Air and atomized water were mixed and heated to 250 C, which killed any micro organisms present in the mixture. The air-steam mixture, thermostatically controlled, was then cooled to 90 F, which permitted the excess water to precipitate out and insured saturation of the air. This sterile and moisture-laden air was then forced into the chamber at the rate of 200 cubic feet (566 cubic meters) per minute or, roughly, four complete changes of air per minute. The chamber was equipped with a false bottom which permitted daily cleaning.

Studies by Smith and Moise,² Sauerbruch³ (on man), Carrel and Baker,¹¹ Osborne and Mendel,⁴ Herrmannsdorfer⁵ (on man), Harvey and Howes⁶ and

† Dr Risk died March 21, 1938

From the Physiological Laboratories, the University of Chicago

1 (a) Carrel, A. Leukocytic Trephones, J A M A **82** 255 259 (Jan 2, 1924) (b) Carrel, A., and Baker, L E J Exper Med **44** 503 1926

2 Smith, A H, and Moise, T S J Exper Med **40** 209, 1924

3 Sauerbruch, F Munchen med Wchnschr **71** 1299, 1924

4 Osborne, T B, and Mendel, L B J Biol Chem **69** 661 1927

5 Herrmannsdorfer, A Deutsche Ztschr f Chir **200** 534 1927

6 Harvey, S C, and Howes, E L Ann Surg **91** 641, 1930

Reimers and Winkler⁷ indicated that a high protein diet accelerates wound healing, whereas a high carbohydrate, fat or vegetable diet markedly inhibits repair. The diet which seemed most satisfactory for this experiment consisted of raw meat, malted milk and a commercially prepared mixture (Purina fox chow^{7a}). An excess of food and water was kept in both the experimental and the control cages at all times.

The lesions were produced by a brass branding iron 10.8 cm square, weighing 240 Gm and heated to the temperature of boiling castor oil (240 C). The iron was placed on the shaven back of the etherized rat for 20 seconds at constant pressure (the weight of the iron). The heat penetrated the corium, producing a third degree burn.

The rats, all mature and weighing about 280 Gm, were then divided into two sets. One set was placed in the humidity chamber (box) while the other was placed in standard wire false bottom cages at room temperature and treated

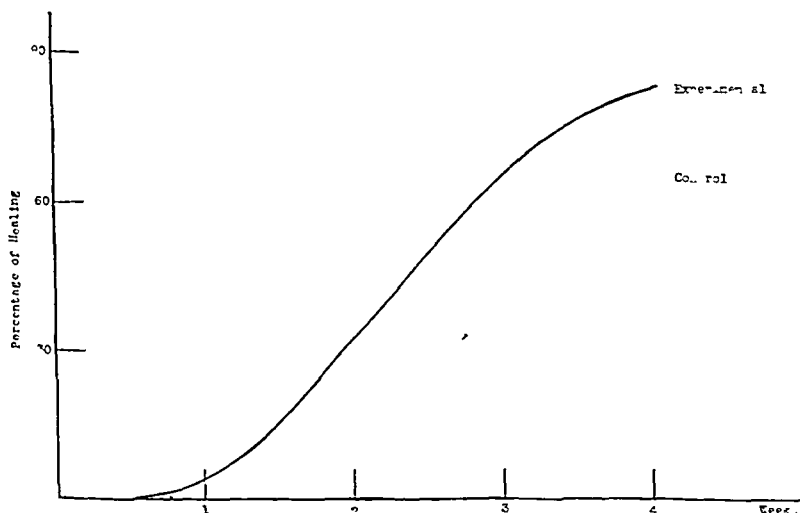


Fig 1 (experiment 1) —Rate of healing of deep cutaneous burns in 10 experimental and 7 control rats treated with butesin picrate ointment three times daily.

in several ways generally acceptable to the members of the medical profession. The two groups were designated respectively as the experimental and the control set.

RESULTS

Figure 1 indicates the comparative rates of healing based on averaged biweekly measurements of the reduction of the injured area. Owing to the presence of debris and coagulum in the controls' healing for the first week cannot be measured accurately. (The percentile rate of healing [ordinate] is plotted against time in

⁷ Reimers C and Winkler H. *Deutsche Ztschr f Chir* **241** 313, 1933.

^{7a} Purina fox chow is composed of the following ingredients: Carotene, dried malt, corn grits, alfalfa meal, ground oat groats, wheat germ, barley, malt molasses, dried skim milk, 1 per cent iodized salt and cod liver oil. Guaranteed analysis: protein 20 per cent (not less), fat 3 per cent (not less), fiber, 6 per cent (not more), nitrogen-free extract 46 per cent.

weeks [ib idem]). The experiment was terminated at the beginning of the fourth week when the experimental rats, which received no other therapy than the heat and humidity of the box, were 82 per cent healed. The control rats, treated with butesin picrate ointment three times daily during the same period, were 63 per cent healed, a difference of 19 per cent in favor of the warmth and humidity

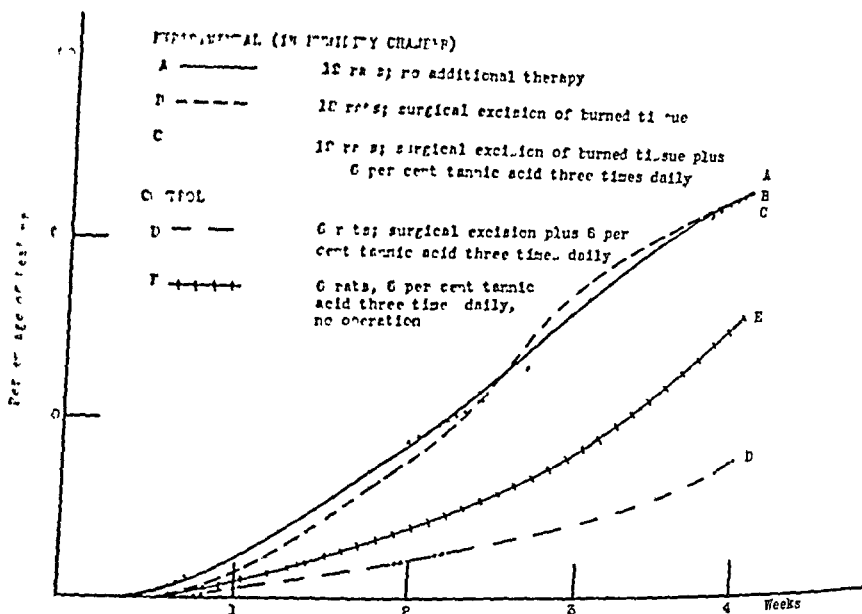


Fig 2 (experiment 2)—Comparative rates of healing with different types of therapy



Fig 3—A, experimental rat treated with surgical excision of the burned tissue plus heat and humidity, B, control rat treated with surgical excision of the burned tissue and no other therapy

Figure 2 illustrates the comparative rate of healing for rats when tannic acid therapy alone and surgical excision of debris plus application of tannic acid were used on groups in both the experimental and the control set.

In this study groups A, B and C composed the experimental set and groups D and E the control set. Group A received no additional therapy. In group B...

burned tissue was surgically excised. In groups C and D the burned tissue was excised and 6 per cent tannic acid used three times daily. Group E received the tannic acid treatment without the surgical excision. Despite the variation in the additional therapy used on the various animals in the experimental set, all rats at the fourth week were 70 per cent healed, in contrast to the two control groups, the rats in group D, which received 6 per cent tannic acid three times daily in addition to surgical excision of the debris, were 24 per cent healed, and those in group E, receiving 6 per cent tannic acid three times daily but without surgical excision of the debris, were 48 per cent healed.

It would seem from these data that surgical excision and surgical excision plus application of tannic acid, when used in conjunction with warmth and humidity, provide no additional stimulus to repair. It does seem that in the case of the control rats the use of tannic acid alone was better therapy than surgical removal of the debris followed by spraying with tannic acid.

Figure 3 illustrates the comparative rates of healing in the experimental and in the control rats when the burned area was surgically excised and no additional therapy given.

COMMENT

Among the many physiologic factors which might account for these results may be listed the following:

- 1 Healing processes are markedly slowed in the presence of debris (Bauer,⁸ Hauberisser,⁹ Dressel¹⁰). In the humidity chamber the moisture of the air kept the entire body wet, and this soaking action softened the debris, which was sloughed off the wound or picked off by the rats within the first five days.

- 2 Increase of local temperature by thermal application increases the rate of healing in rats (Fuks¹¹). Ebeling,¹² using the alligator, made the same observation. In the humidity chamber the warmth provided exceeded the normal temperature of the skin.

- 3 Epithelial proliferation is faster in the presence of moisture (Burrows,¹³ 1924). The saturated air of the humidity chamber not only provides moisture but permits retention of water, for evaporation is minimal in saturated air.

- 4 Chief among the many factors that delay wound healing is infection (Carrel, Kiser¹⁴). According to a report by Schade and Claussen,¹⁵ the p_H of tissue may be a prime factor in the incidence of pathogenic invasion. These investigators, working with the quinhydrone electrode, found that healthy granulating tissue had a p_H of 5.6 but that if the

8 Bauer K. H. Arch f klin Chir **163** 564 1931

9 Hauberisser, E. Beitr z klin Chir **153** 257, 1931

10 Footnote deleted on proof

11 Fuks T. Jap J Obst & Gynec **15** 234 1932

12 Ebeling A. H. J Exper Med **35** 657 1922

13 Burrows, M. T. J M Research **41** 615 1924

14 Kiser S. Arch f klin Chir **149** 146 1927

15 Schade H. and Claussen F. München med Wchnschr **73** 343 1926

tissue became dry the p_{H} rose to 8.3. If the alkalinity persisted infection and sloughing occurred. Reimers and Winkler⁷ reported that carbon dioxide escapes from the surface of wounded tissue thirty times as fast as from uninjured skin. The fact that Reimers and Winkler reported a rising p_{H} coinciding with drying of the tissue suggests the possibility that moisture may act as a vehicle in the retention of the acid radicals responsible for the lowered p_{H} .

As for the tannic acid or butesin picrate ointment, we believe on the basis of the evidence obtained in experiment 2 that these substances possess no specific accelerative healing action. It would seem that their main function is to provide an insoluble coagulant over the wound. The incidence of infection under the coagulant produced by tannic acid has been reported many times and constitutes the chief objection to the use of the medicament.¹⁶

SUMMARY

Deep cutaneous burns were inflicted on etherized rats. Studies of recovery with various types of therapy or lack of therapy were undertaken. The speed of healing constituted the criterion of recovery. The results of the experiments were as follows:

- 1 The cutaneous burns of rats receiving the warm moist air therapy, healed faster than those of controls living in ordinary air at room temperature, even when the controls received in addition typical treatments with well known therapeutic agents (butesin picrate and tannic acid).
- 2 The use of tannic acid and surgical excision in addition to the warm moist air therapy did not produce significant differences in the rate of healing in the experimental rats.
- 3 Surgical excision of the debris in the control group of rats was better than no therapy but was inferior to the chemical coagulants present in tannic acid or butesin picrate ointment.

Dr. A. J. Carlson gave assistance and criticism in this work.

¹⁶ Turner, A. C. Contribution to Treatment of Burns, *Brit. M. J.* 2: 99, (Nov. 23) 1935. Taylor, F. Misuse of Tannic Acid *J. A. M. A.* 106: 1144, 1146 (April 4) 1936.

ETIOLOGY OF GALLSTONES

A CRITICAL SURVEY OF THE LITERATURE AND A STUDY OF THE
APPLICABILITY OF VARIOUS THEORIES IN TWO HUNDRED
AND THIRTY-NINE OPERATIVE CASES

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Study as to the cause of gallstones has been extensive since they were first reported in the fourteenth or the fifteenth century. Early thought was purely speculative, but since the time of Naunyn a mass of clinical and experimental data has been accumulated. A multitude of theories have been propounded none of which is adequate to explain the whole problem.

A fundamental difficulty has been the failure to recognize that the conditions which determine the formation of biliary calculi are multiple and complex. In addition there are several varieties of gallstones. According to the classification of Naunyn there are pure cholesterol stones, calcium bilirubinate stones and the common "mixed" gallstones. Each of these may be determined by the combination of a different set of circumstances. In the series of observations we shall discuss only the pure cholesterol stone and the common "mixed" gallstone will be considered.

The cause of gallstones must be sought among many factors. These factors resolve themselves generally into two groups. The first is related to changes in the composition of the hepatic bile, whether due to aberrations in the general metabolism (hypercholesteremia, diet, systemic disease or pregnancy) or to disease or injury of the liver. The second group is related to changes taking place directly in the gall-bladder or bile ducts and favoring the formation of calculi.

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The metabolic theory, which assumes that disturbances in metabolism so change the hepatic bile as to predispose to the formation of concretions, has been brought forward to explain the formation of pure cholesterol stones. It is equally applicable, however, to explain the formation of pigment stones. Giffin,¹ in particular, has emphasized the frequency of gallstones (58 per cent) in adults with congenital hemolytic jaundice. These stones characteristically are hard brown or black pigment stones consisting of bilirubin and calcium bilirubinate. They are apparently related to the pleocholia, or excessive excretion of bile pigment, associated with this condition. Greene and Snell² found experimentally that an augmented rate of excretion of pigment in the bile is brought about primarily by an increase in concentration rather than by an increase in the volume of the bile. Pleocholia, therefore, may well predispose to the deposition of this particular form of calculus.

The metabolic theory is usually restricted to the formation of cholesterol stones. As advocated by Chauffard and his co-workers,³ it assumed a correlation between the concentration of cholesterol in the blood and that in the bile and so maintained that an elevated value for blood cholesterol is a predisposing factor in the formation of gallstones. The clinical experience of Chauffard, Moynihan,⁴ Hansen,⁵ Dewey⁶ and others seemingly has substantiated this belief. The observation of an increased concentration of cholesterol in both the blood and the bile during pregnancy, the frequent onset of clinical symptoms during or immediately after pregnancy and the higher incidence of gallstones in women than in men have all been factors in the acceptance of this theory. Dietary experiments with animals, with the use of diets rich in cholesterol, have demonstrated that the cholesterol content of the blood can be increased markedly by each feeding. This finding has received added confirmation by the work of Wilensky⁷ and of Roth-

1 Giffin, H. Z. Hemolytic Jaundice. A Review of Seventeen Cases, *Surg Gynec & Obst* **25** 152 (Aug) 1917.

2 Greene, C. H., and Snell, A. M. Studies in the Metabolism of the Bile. II. The Sequence of Changes in the Blood and Bile Following the Intravenous Injection of Bile and Its Constituents, *J Biol Chem* **78** 691 (Aug) 1928.

3 Chauffard, A. Role of Hypercholesterolemia in Pathogenesis of Gall Stones, *J med franç* **26** 251 (Aug) 1927. Chauffard, A., Laroche, G. and Grigaut, A. Le taux de la cholestérolémie chez les hépatiques, *Compt rend Soc de biol* **70** 20, 1911.

4 Moynihan, B. Some Aspects of Cholelithiasis, *Brit M J* **1** 393 (Feb 2) 1925.

5 Hansen, S. Die Bedeutung des Cholesterins für die Bildung von Gallsteinen durch experimentelle Untersuchungen beleuchtet, *Acta chir Scandnav* **62** 483, 1927.

6 Dewey, K. Experimental Hypercholesterolemia, *Arch Int Med* **17** 77 (June) 1916.

7 Wilensky, A. O. Hypercholesteremia, *Surg, Gynec & Obst* **35** 1 (Feb) 1924.

child and Wilensky,⁵ Walsh,⁹ Walsh and Ivy,¹⁰ and Andrews, Hrdina and Dostal,¹¹ Riegel, Ravdin and Rose,¹² Patey,¹³ and many others, however, were unable to find such a definite relation between the cholesterol content of the blood and that of either hepatic or gallbladder bile either in patients or in experimental animals. They therefore concluded that there is no direct relation between the cholesterol content of the blood and the formation of gallstones.

The bile salts in hepatic bile are the specific secretion of the liver cells and numerous investigators, such as Stadelmann,¹⁴ Whipple,¹⁵ Ivy,¹⁶ Doubilet,¹⁷ Greene, Walters and Frederickson,¹⁸ have shown that this excretion in the bile is an extremely sensitive index of the functional activity of the hepatic parenchyma. The bile salts also have a role in keeping the cholesterol of the bile in solution. Changes in the functional activity of the liver from hepatitis, suppression of secretion or metabolic disturbances may so change the concentration of bile salts in the hepatic bile as to favor the precipitation of cholesterol. The importance of this bile salt-cholesterol ratio in the formation of gallstones will be discussed later in this paper. Excretion of bacteria, bile thrombi or abnormal toxic products due to hepatic damage and other organic changes in the liver and its secretion have been suggested

8 Rothschild, M. A., and Wilensky, A. O. Studies in Cholelithiasis. I. The Disturbances of the Cholesterol Metabolism as a Factor in Gall Stone Formation, *Am J M Sc* **156** 139 (Aug.) 1918, II. The Clinical Relationships of Cholesterinemia to the Pathological Process, *ibid* **156** 404 (Sept.) 1918.

9 Walsh, E. L. The Etiology of Gall Bladder Calculi, *Arch Path* **15** 698 (May) 1933.

10 Walsh, E. L., and Ivy, A. C. Observations on the Etiology of Gall Stones, *Ann Int Med* **4** 134 (Aug.) 1930.

11 Andrews, E., Hrdina, L., and Dostal, E. Etiology of Gall Stones. II. Analysis of Duct Bile from Diseased Livers, *Arch Surg* **25** 1081 (Dec.) 1932.

12 Riegel, C., Ravdin, I. S., and Rose, H. Studies of Gall Bladder Function. VI. Cholesterol in Human Liver Bile, *J Clin Investigation* **16** 67 (Jan.) 1937.

13 Patey, D. H. Modern Views on Mechanism of Formation of Gall Stones, *Brit M J* **1** 866 (May 20) 1933.

14 Stadelmann, E. *Der Icterus und seine verschiedenen Formen*. Stuttgart: Ferdinand Enke, 1891.

15 Whipple, G. H. Origin and Significance of Constituents of the Bile, *Physiol Rev* **2** 440 (July) 1922.

16 Ivy, A. C. Factors Concerned in the Evacuation of the Gall Bladder, *Medicine* **11** 345 (Sept.) 1932.

17 Doubilet, H. Hepatic Excretion in Man of the Various Bile Acids Following Their Oral Administrations, *Proc Soc Exper Biol & Med* **36** 50 (Feb.) 1937.

18 Greene, C. H., Walters, W., and Frederickson, C. H. The Composition of the Bile Following the Relief of Biliary Obstruction, *J Clin Investigation* **9** 295 (Oct.) 1930.

repeatedly as forming the nuclei for stones Crile¹⁹ concluded that energy changes in the body, affecting the liver and causing abnormality of the bile, result in the formation of stones and that these in turn cause the infection frequently seen in calculous gallbladders He stated "Our thesis is that the chemical and physical basis of gallstones is laid by changes in the secretion of the biologically active liver cells and not by changes in the sac that holds and concentrates the bile and performs no other function"

By means of ingenious experiments in which the common duct was catheterized under completely aseptic conditions, Rous, McMaster and Drury²⁰ have shown the formation of stones without any evidence of stasis infection or changes in the composition of the blood They concluded from this experimental work that stones may form from altered hepatic secretion Rovsing²¹ came to a similar conclusion

Attempts to show a relation between the intake of fluids and the volume of bile secreted by the liver have been unsuccessful Of seemingly greater significance is the recognized importance of the changes occurring in bile during its passage through the bile ducts and gallbladder It is here that the controversy concerning the physiologic action of the gallbladder becomes of major importance in evaluating theories concerning the formation of gallstones The question is Does the normal gallbladder absorb cholesterol, as has been maintained by Policard,²² Whitaker,²³ Mentzer,²⁴ Boyd,²⁵ Halpert,²⁶ Sweet²⁷ and others, does it secrete cholesterol, as has been contended by Elman

19 Crile, G Energy Background of Genesis of Gall Stones and of Prevention of Immediate Post-Operative Shock and of Later Digestive Disturbances, Surg, Gynec & Obst **60** 818 (April) 1935

20 Rous, P, McMaster, P D, and Drury, D R Observations on Some Causes of Gall Stone Formation I Experimental Cholelithiasis in the Absence of Stasis, Infection and Gall Bladder Influences, J Exper Med **39** 77 (Jan) 1924
Rous, P, Drury, D R, and McMaster, P D II On Certain Special Nuclei of Deposition in Experimental Cholelithiasis, *ibid* **39** 97 (Jan) 1924

21 Rovsing, T Gall Stones Cause, Not Result, of Infection, Acta chir Scandinav **56** 103, 1923

22 Policard, A Sur quelques donnees histo-physiologiques concernant le mecanisme fonctionnel et pathologique et de la vesicule et des voies biliaires, J von chir **19** 799, 1922

23 Whitaker, L R The Relation of Biliary Dysfunction to Lithiasis, N York State J Med **34** 221 (March 15) 1934

24 Mentzer, S H A Clinical and Pathological Study of Cholecystitis and Cholelithiasis, Arch Surg **14** 14 (Jan) 1927

25 Boyd, W Studies in Gall-Bladder Pathology, Brit J Surg **10** 337 (Jan) 1923

26 Halpert, B The Gall Bladder in the Light of Recent Investigation, N Surg **19** 1037 (Dec) 1929

27 Sweet, J E The Formation of Gall Stones, Am J Surg **40** 172 (April) 1938

and Graham²⁸ and originally by Naunyn,²⁹ or does it normally only concentrate cholesterol, as the observations and experimental data of Ravdin and Johnston,³⁰ Walsh⁹ and Andrews Schoenheimer and Hrdina³¹ indicate? Lichtwitz,³² in 1914, further complicated the question by suggesting that saturation of the plicae of the gallbladder with cholesterol (by absorption from the bile) and their subsequent dehiscence form the nuclei for "metabolic" stones. Though this theory has been supported recently by Gosset, Bertrand and Loewy,³³ it has been denied by Illingworth³⁴ and Mackey.³⁵

It is generally agreed that the gallbladder extracts water as well as sodium chloride and other inorganic salts from the hepatic bile, concentrating it from seven to ten times (Ravdin and Johnston³⁰ and others). It would appear from clinical and experimental studies that while the mucosa of the gallbladder may absorb bile salts or cholesterol from the bile this does not occur under normal circumstances. In the presence of an inflammation, when the mucosa is edematous, Dostal and Andrews³⁶ have shown that bile salts are rapidly absorbed by the wall of the gallbladder. Clinically this is seen most readily in cases of hydrops of the gallbladder. Another explanation is that advanced by Rous, McMaster and Drury²⁰ in the replacement of the bile (including cholesterol and bile salts) by mucus, which is a specific response of the mucosa of the gallbladder. Aronsohn and Andrews³⁷ have demon-

28 Elman, R, and Graham, E. The Pathogenesis of "Strawberry" Gallbladder (Cholesterosis of the Gallbladder) *Arch Surg* **24** 14 (Jan.) 1932

29 Naunyn, B. *Klinik der Cholelithiasis*, Leipzig, F. C. W. Vogel, 1892, A Treatise on Cholelithiasis, London New Swedenham Society 1896

30 Ravdin, I. S., and Johnston, C. G. Gallbladder. Recent Advances as Applied to Treatment, *Pennsylvania M J* **35** 357 (March) 1932. Ravdin, I. S., Johnston, C. G., Austin, J. H. and Riegel, C. Studies of Gall-Bladder Function. Absorption of Chloride from Bile-Free Gall Bladder, *Am J Physiol* **99** 638 (Feb.) 1932

31 Andrews, E. Schoenheimer, L. R., and Hrdina, L. Etiology of Gall Stones. Clinical Factors and Role of Gall Bladder, *Arch Surg* **25** 796 (Oct.) 1932

32 Lichtwitz, L. Ueber die Bildung der Harn und Gallensteine. *Ergebn d inn Med u Kinderh* **13** 1 1914. Zur Genese der Gallensteine, *München med Wchnschr* **55** 629 1908

33 Gosset, A. Bertrand, I., and Loewy, G. La vesicule traïse, *Progres med* **41** 1792 (Oct. 30) 1928

34 Illingworth, C. F. W. Cholesterosis of the Gall-Bladder. Clinical and Experimental Study. *Brit J Surg* **17** 205 (Oct.) 1929

35 Mackey, A. Cholesterosis of the Gall Bladder. *Brit J Surg* **24** 570 (Jan.) 1937

36 Dostal, L. E. and Andrews, E. Etiology of Gall Stones. Effect of Diet on the Bile Salt Cholesterol Ratio. *Arch Surg* **26** 258 (Feb.) 1933

37 Aronsohn, H. G. and Andrews, E. Experimental Cholecystitis, *Surg Gynec & Obst* **66** 748 (April) 1938

strated that chemical cholecystitis may be set up by a high concentration of bile salts in the gallbladder and possibly in the blood stream. How, then, may one account for the concentration of cholesterol which may be found in gallbladder bile—100 to 2,000 mg per hundred cubic centimeters? The hepatic bile contains little cholesterol, yet from ten to one hundred times its concentration is often seen in the gallbladder at operation, whereas the concentration of bile salts is seldom above ten times the concentration in the hepatic bile. While this finding may be cited as evidence that the cholesterol is secreted by the mucosa of the gallbladder, the work of Boyd²⁵ Whitaker,²³ Sweet³⁸ and Wilkie and Doubilet³⁹ opposes such an assumption.

It is agreed that some, if not all, of the cholesterol in the bile is in a state of colloidal solution. The studies of Wieland and Sorg⁴⁰ showed that the bile salts, particularly the salts of desoxycholic acid form addition compounds with fatty acids or cholesterol which increase the solubility of the latter. Verzar and Kúthy,⁴¹ in particular, have stressed the importance of such compounds in favoring the intestinal absorption of lipoids and cholesterol. Other investigators, following Newman,⁴² have stressed the importance of these compounds in keeping the cholesterol in the bile solution and have insisted that when the bile salt-cholesterol ratio falls below a critical level cholesterol is precipitated out of solution. It is further assumed that such precipitation leads to the formation of cholesterol calculi.

The bile salt-cholesterol ratio may be disturbed either by hepatic damage with a changed hepatic bile or by a differential absorption of cholesterol and bile salts in the gallbladder or bile ducts. Hammarsten⁴³ reported the bile salt-cholesterol ratio in the normal gallbladder to be 25:1. Newman,⁴² who first emphasized the importance of this ratio in the pathogenesis of gallstones, stated that the critical ratio for

38 Sweet, J. E. The Liesegang Phenomenon in Gall Stones, in Weiser, H. B. Colloid Symposium Annual, New York, John Wiley & Sons, Inc., 1930, p. 249, Formation of Calculi, *Ann Surg* **101** 624 (Jan.) 1935.

39 Wilkie, A. L., and Doubilet, H. Passage of Cholesterol Through the Mucosa of the Gallbladder, *Arch Surg* **26** 110 (Jan.) 1933.

40 Wieland, H., and Sorg, H. Untersuchungen über die Gallensauren Zettel f. physiol. Chem. **97** 1, 1916.

41 Verzar, F., and von Kúthy, A. Die Bedeutung der Gallensauren für die Fettresorption, *Biochem. Ztschr.* **205** 369, 1929, Die Bedeutung der gepaarten Gallensauren für die Fettresorption, *ibid.* **230** 451, 1931. Verzar, F. Absorption of Fats, *Nutrition Abstr. & Rev.* **2** 441 (Jan.) 1933.

42 Newman, C. Physiology of the Gall Bladder and Its Functional Abnormalities (Goulstonian Lecture), *Lancet* **1** 785 (April 15), 896 (April 29) 1933.

43 Hammarsten, O. Darstellung der Gallensauren und ihrer wichtigsten Abbauprodukte und ihr Nachweis, in Abderhalden, E. *Handbuch der biologischen Arbeitsmethoden*, Berlin, Urban & Schwarzenberg, 1925, pt. 6.

the precipitation of cholesterol is 18:1. Andrews, Schoenheimer and Hrdina³¹ placed the critical ratio at 13:1. Walsh and Ivy,³⁰ Walsh⁹ and Dolkart, Jones and Brown,⁴⁴ in exhaustive experimental studies, have shown that fatty acids have a solvent action on cholesterol masses and on "mixed" gallstones. They concluded therefore, that it is the concentration of fatty acids in the bile rather than that of bile salts that keeps the cholesterol in solution. Illingworth³⁴ Reinhold, Ferguson and Hunsberger⁴⁵ and Weiser and Gray,⁴⁶ on the other hand, did not attach significance to the presence of fatty acids, for they were unable to demonstrate fatty acids in bile from normal gallbladders in sufficient concentration to prevent the precipitation of cholesterol.

Phemister and his associates⁴⁷ reported that precipitates of calcium salts are formed in gallbladders only when a complete obstruction and a low grade chronic inflammation are present. They argued that since cholesterol is not found in such gallbladders the gallbladder cannot be the source of the cholesterol found in gallstones. Calcium salts they concluded, represent a specific response on the part of the wall of an inflamed gallbladder.

Reported changes in the reaction of bile have not been consistently demonstrated in calculous gallbladders. Feldman, Morrison and Krantz⁴⁸ reasoning from the observation that human cholesterol and "mixed" gallstones will dissolve when placed in the more acid gallbladder bile of the dog, concluded that the alkaline p_H of human hepatic bile unchanged by the gallbladder, may be an important etiologic factor in the formation of gallstones. Reinhold, Ferguson and Hunsberger,⁴⁵

44 Dolkart, R. E., Jones, K. K., and Brown, C. F. G. Chemical Factors Concerned in the Formation of Gallstones, *Arch. Int. Med.* **62**: 618 (Oct.) 1938. The Relation of the Hydrogen Ion Concentration of Bile to the Formation of Gall Stones, *Am. J. Digest. Dis. & Nutrition* **4**: 587 (Nov.) 1937.

45 Reinhold, J. G., Ferguson, L. K., and Hunsberger, A. Composition of Human Gall Bladder Bile and Its Relationship to Cholelithiasis, *J. Clin. Investigation* **16**: 367 (May) 1937.

46 Weiser, H. B., and Gray, G. R. Mechanism of Formation of Pure Cholesterol Gall Stones. *Arch. Path.* **17**: 1 (Jan.) 1934.

47 Phemister, D. B., Aronsohn, H. G., and Pepinsky, R. Variation in Cholesterol, Bile Pigment and Calcium Salts Contents of Gallstones Formed in Gallbladder and in Bile Ducts with the Degree of Associated Obstruction, *Ann. Surg.* **109**: 161 (Feb.) 1939. Phemister, D. B., Dav, L., and Hastings, A. B. Calcium Carbonate Gallstones and Their Experimental Production. *Ann. Surg.* **96**: 595 (Oct.) 1932.

48 Feldman, M., Morrison, S., and Krantz, I. C. Jr. Etiology of Gall Stones. Relationship of p_H of Bile to the Formation and Dissolution of Gall Stones, *Am. J. Digest. Dis. & Nutrition* **4**: 13 (March) 1937. Feldman, M., Morrison, S., Carr, C. I., and Krantz, I. C. Jr. Contribution to the Etiology of Gall Stones. A Study of the Hydrogen-Ion Concentration of Gall Bladder Bile and Its Effect upon Gall Stones. *ibid.* **4**: 223 (June) 1937.

Reinhold and Ferguson,⁴⁹ Rous⁵⁰ and Weiser and Gray,⁴⁶ on the other hand, did not find that normal gallbladder bile has a higher hydrogen ion concentration than hepatic bile. They stated the belief that there is no marked change in the presence of an inflammation. Walsh⁵² reported that an acid pH allows cholesterol to stay in solution more readily but ascribed this to the presence of bile acids and to fatty acids which are known solvents of cholesterol. Dolkart, Jones and Brown⁴⁴ found no statistically significant difference in the relative solvent action on mixed stones of acid and alkaline bile secured from the ox, the dog or man.

The original hypothesis of Naunyn,²⁹ propounded in 1892, held that gallstones are the result of an infection in the gallbladder or bile ducts. Nearly all subsequent theories have presupposed that some injury, inflammation or chemical change of the bile in the gallbladder is the initiating cause for the formation of stones. Moynihan⁴ has stated "the gall stone is a tombstone erected to the memory of the organism within it." The early clinical researches indicated that most gallbladders with stones are infected. Gordon-Taylor and Whitby⁵¹ found 70 per cent infected, Moynihan found 95 per cent infected, and Walton⁵² found 70 per cent infected. Recent clinical studies by various investigators have shown wide variation in the incidence of bacteria-yielding cultures of material from calculous gallbladders. Moynihan,⁴ Griffith and Kipp,⁵³ Patey,¹³ Walton,⁵² Albeaux-Fernet⁵⁴ and Walters,⁵⁵ as well as many others, have concluded from a clinical standpoint that infection of the gallbladder is a basic cause for stone formation, since it causes changes in the mucosa with resulting functional disturbances, stasis and colloidal changes favoring precipitation. All have agreed that pure cholesterol stones are metabolic in origin, thus differing from the mixed, or common, gallstones. Potter and Mann,⁵⁶ Illing

49 Reinhold, J. G., and Ferguson, L. K. Reaction of Human Bile and Its Relationship to Gall Stone Formation, *J. Exper. Med.* **49** 681 (April) 1929.

50 Rous, P. Physiological Factors in the Genesis of Gall Stones, *Proc. Inst. Med. Chicago* **7** 33 (April 15) 1928.

51 Gordon-Taylor, G., and Whitby, L. E. H. A Bacteriological Study of Fifty Cases of Cholecystectomy with Special Reference to Anaerobic Infection, *Brit. J. Surg.* **18** 78 (July) 1930.

52 Walton, J. The Formation and Treatment of Calculi in the Biliary Ducts and Gall Bladder, *Surg., Gynec. & Obst.* **64** 257 (Feb.) 1937.

53 Griffith, J. P., and Kipp, H. A. Remarks on the Etiology and Treatment of Cholecystitis, *Pennsylvania M. J.* **35** 362 (March) 1932.

54 Albeaux-Fernet, M. Les hypotheses pathogeniques de la lithiase biliaire, *Gaz. med. de France (suppl. Gastro-enterol.)* [43] 3 (Nov. 15) 1936.

55 Walters, W. Pathological Physiology of Stone in the Common Bile Duct, *Clinical and Surgical Significance*, *Surg., Gynec. & Obst.* **63** 417 (Oct.) 1936.

56 Potter, J. C., and Mann, F. C. Pressure Changes in the Biliary System, *Am. J. M. Sc.* **171** 202 (Feb.) 1926.

worth,⁵⁷ Ravdin and Johnston³⁰ and Furth⁵⁸ have reached the same general conclusion after animal experimentation and clinical studies. Illingworth stated the belief that the Lichtwitz³² theory of electropositive and electronegative charges, with the inflammatory exudate acting as an electronegative substance, may explain the "trigger mechanism" which causes the cholesterol to precipitate.

On the other hand Aschoff and Bacmeister,⁵⁹ Rovsing²¹ and Crile,¹⁹ after both clinical and experimental studies, concluded that the infection is the consequence and not the cause of gallstones. MacCarty⁶⁰ made a statistical study of 21,523 gallbladders but was unable to determine which is the primary factor, whereas Walters⁵³ and Ravdin and Johnston³⁰ stated the belief that either may be the initial condition. It is debatable, therefore, whether this question can be answered by clinical research alone.

Aschoff and Bacmeister's assumption that neither infection nor a product of infection is the cause of stones arose from their experimental and clinical studies on the precipitation of cholesterol in the presence of stasis within the gallbladder. They maintained that this stasis, regardless of the cause, favors changes in solubility due to over-concentration of the cholesterol with resultant precipitation, the precipitated cholesterol being the nucleus of the stone. The fact that many pathologic conditions, some of them neurogenic, result in biliary stasis and an increased concentration of the bile within the gallbladder has been established by Westphal⁶¹, Ivy,¹⁶ Whitaker²³ and Greene, Twiss and Carter.⁶² Though McMaster and Elman,⁶³ Boyden,⁶⁴ Whitaker⁶⁵

57 Illingworth C F W. The Formation of Calculi, Edinburgh M J 43 481 (Aug) 1936

58 Furth O. Pathologische Physiologie der Aufbau der Gallensteinen, Wien klin Wchnschr 50 629 1937

59 Aschoff L and Bacmeister, A. Die Cholelithiasis, Jena, Gustav Fischer, 1909. Lectures on Pathology, New York, Paul B Hoeber, 1924

60 MacCarty W C. The Gallbladder and Its Diseases, Proc Staff Meet, Mayo Clin 11 805 (Dec 16) 1936

61 Westphal K. Muskelfunktion, Nervensystem und Pathologie der Gallenwege. Ztschr f klin Med 96 22 1923. Die Bewegungs- und Resorptionsstörungen in den Gallenwegen und ihre Gefahren, Verhandl d deutsch Gesellsch f inn Med 1932 Knog 44 p 354

62 Greene C H, Twiss I R and Carter R F. Biliary Stasis, Am J Digest Dis & Nutrition 3 622 (Nov) 1936

63 McMaster P D and Elman R. On the Expulsion of Bile by the Gall Bladder and a Reciprocal Relationship with the Sphincter Activity, J Exper Med 44 173 1926

64 Boyden E A. Sphincter of Oddi in Man and Certain Representative Mammals. Surgery 1 25 (Jan) 1937

65 Whitaker L R. The Mechanism of the Gallbladder and Its Relation to Cholelithiasis. J A M A 88 1542 (May 14) 1927

and Ravdin and Johnston⁷⁰ could demonstrate no definite reciprocal relation between the sphincter of Oddi and the gallbladder of the dog, according to Berg and Jobling,⁶⁶ Ivy¹⁶ and Meltzer⁶⁷ there is much indirect evidence that such a relation does exist

Whitaker⁶⁸ has demonstrated the formation of pseudostones in the gallbladder of the dog by inducing stasis in the absence of infection or damage to the liver. Meltzer,⁶⁷ von Babarczy⁶⁸ and Halpert⁶⁹ have also made a strong case for stasis. Ravdin and Johnston,³⁰ Walters,⁷¹ Walsh,⁷² Moore⁷⁰ and also Rous⁵⁰ have shown that stasis is at least an accessory factor in the formation of stones. Cooper and Illingworth⁷¹ were unable to reproduce Whitaker's experimental results and so agreed with Pavel,⁷² Furth⁵⁸ and many others that stasis is not a probable cause for the formation of gallstones.

The observation that pure cholesterol stones crystallize according to the laws of colloids has led to the "colloidal theory" of stone formation, supported extensively by Sweet,³⁸ Weiser and Gray⁴⁶ and Shade.⁷³ Sweet maintained that "under normal conditions, whatever passes into the gallbladder through the cystic duct, never passes out again through the cystic duct." He made synthetic stones from gelatin, chromates and silver nitrate and found them to be structurally similar to the cholesterol stones in the human gallbladder. The Liesegang phenomenon, with rhythmic precipitation of calcium and pigment, he concluded, explains the laminated appearance on section of cholesterol and mixed gallstones. Phemister and his associates,⁴⁷ on the other hand, insisted that the deposition of calcium is evidence of inflammatory changes in the wall of the gallbladder. They stated that when a gallstone consists of a

66 Berg, B. N., and Jobling, J. W. The Effect of Division and Transplantation of the Common Duct upon the Gall Bladder Function, *Proc Soc Exper Biol & Med* **24** 434 (Feb.) 1927. Berg, B. N. Gall Bladder Function After Division of the Common Duct, *Surg., Gynec & Obst* **46** 464 (April) 1927.

67 Meltzer, S. J. The Disturbance of the Law of Contrary Innervation as a Pathologic Factor in Diseases of the Bile Ducts and the Gall Bladder, *Am J M Sc* **153** 469 (April) 1917.

68 von Babarczy, M. Die Bedeutung der Cholesterins in der Diagnostik der Cholecystopathien, *Ztschr f klin Med* **133** 656, 1938.

69 Halpert, B. New Aspects of Formation and Classification of Gall Stones, *Arch Path* **6** 623 (Oct.) 1928.

70 Moore, S. W. Intramural Formation of Calculi, *Arch Surg* **31** 416 (March) 1937.

71 Cooper, G. H., and Illingworth, C. F. W. Experimental Study of the Factor of Biliary Stasis in the Production of Gall Stones, *Surg., Gynec & Obst* **46** 658 (May) 1928.

72 Pavel, I. Du rôle peu important de la stase dans la pathogenèse de la lithiase biliaire (avec une critique de la dyskinesie et quelques conclusions thérapeutiques), *Presse med* **43** 1565 (Oct 9) 1935.

73 Shade, H., cited by Sweet³⁸

central nucleus of cholesterol with several rings of calcium and pigment around the periphery, this structure is evidence for the occurrence of successive attacks of obstruction and active cholecystitis in a gallbladder which initially contained a pure cholesterol stone of metabolic origin. At present these opposing views of Phemister and Sweet are irreconcilable.

Pancreatic ferments have been found in many calculous gallbladders removed at operation, and it has been assumed that the ferments were regurgitated through the common and cystic ducts into the gallbladder. Sweet,⁷² Crile⁷³ and Wolfer⁷⁴ have concluded that this may be a factor leading to the precipitation of cholesterol. Colp, Gerber and Doubilet⁷⁵ stated the belief that such a reflux was the cause of severe acute cholecystitis in 3 cases which they reported. Andrews and his co-workers were able to change the bile salt-cholesterol ratio in the gallbladders of dogs by injecting pancreatic fluid into them. The common finding of pancreatic ferments in gallbladders removed at operation warrants further investigation.

PURPOSE OF THIS STUDY

The present survey was made to see whether in a series of patients with and without gallstones and with either disease or dysfunction of the gallbladder the operative findings could be correlated with the results of a detailed chemical and bacteriologic study in such a way as to throw additional light on the applicability of the different theories of origin of the gallstone. All patients were studied in the clinic for patients with disease of the gallbladder. In the case of each there was a preoperative period of study, pathologic, bacteriologic and chemical examinations were made of the operative specimens and there was careful clinical and laboratory observation during the postoperative period of follow-up.

We recognize that this analysis was made on patients long after the stones had been formed in some instances probably twenty-five years later. It is probable therefore that the factors present at the time the stones were formed were no longer present or active at the time of the study. We can only point out the difficulties of determining the exact pathogenesis of the stones in this or in any similar series of cases and the inapplicability of most of the aforementioned theoretic causes. If it were possible experimentally to produce all types of stones under conditions comparable to those in the human organism or to follow patients before and after the formation of the stones one could more readily solve the problems of their formation.

⁷² Sweet, I. A. Further Evidence That Pancreatic Juice Reflux May Be the Etiologic Factor in Gallbladder Disease. *Ann Surg* **109** 187 (Feb.) 1939.

⁷³ Colp, R., Gerber, I. E. and Doubilet, H. Acute Cholecystitis Associated with Pancreatic Reflux. *Ann Surg* **103** 67 1936.

METHOD AND RESULTS

Duodenal Drainage—During the past nine years, 239 operative cases from the clinic for patients with disease of the gallbladder have been studied in this fashion. In the majority of cases the preoperative period of observation was from one to thirty-six months. In all cases duodenal drainage was done and a chemical examination of the blood was made before operation. Drainage was done according to the method described by Twiss and Phillips.⁷⁶ The duodenal contents were examined for concentration of bile salts, cholesterol content, activity of pancreatic ferment and microscopic evidence of crystals, pus cells and epithelial debris. A bacteriologic examination of the duodenal contents was made. A "fasting gastric specimen" was usually examined for hydrochloric acid content at the beginning or at the completion of the duodenal drainages. Specifically, this study on duodenal drainage was done to correlate the preoperative with the operative findings and to establish any relation which might exist between the material obtained by duodenal drainage and the presence of cholelithiasis.

When the average results found in this series of preoperative duodenal drainages were correlated with the presence or absence of stones (table 1), there was no difference in the bile salt concentration, the cholesterol content and the presence

TABLE 1—Average Results in Specimens Obtained by Duodenal Drainage

	Bile Salts, Mg /100 Cc	Cholesterol, Mg /100 Cc	Percentage with Crystals	Percentage with Organisms
Patients with noncalculous gallbladders	2,000	42	86.2	14
Patients with calculous gallbladders	2,050	39	70.6	4

or absence of crystalline sediment. Evidence of infection in the biliary tract as revealed by culture of the duodenal contents (contaminated specimens excluded) was, however, found in more than half the gallbladders with stones and in only 14 per cent of those without stones.

The presence of crystals has been described as indicative of the presence of stones. That this is a misleading conclusion is apparent when the operative findings in this series of cases are correlated with the results of duodenal drainage. In 24.4 per cent of the patients with stones, no crystals were found in the preoperative duodenal drainage, but crystals were present in 86.2 per cent of the patients without stones. While the presence or absence of crystals has no specific diagnostic import where stones are concerned, their presence is definitely indicative of stasis in the biliary tract. This is particularly evident in patients with dyskinesia of the gallbladder, who frequently show exacerbation of their symptoms at the same time that duodenal drainage shows the presence of crystals.

Blood Chemistry—Preoperative studies of the blood chemistry were made in every case. Repeated studies were done in cases observed for more than one year. This included the determination of the total cholesterol, the cholesterol ester, the icteric index and the van den Bergh reaction. For a time other tests were made.

76 Twiss, J. R., and Phillips, C. H. Bacteriological Findings in Duodenal Drainage, Improved Method of Obtaining Cultures of Bile by Duodenal Drainage, *Am J Digest Dis & Nutrition* 2:663 (Jan) 1935.

function were performed, but these were abandoned in favor of determination of the cholesterol-cholesterol ester ratio, which was studied to estimate the hepatic reserve and to evaluate the role of hypercholesteremia in the formation of gallstones

During the period of preoperative observation (table 2) the average cholesterol content of the blood was equal in patients with stones and in those without. There were wide variations, but when a further analysis was made of those with hypercholesteremia (220 mg per hundred cubic centimeters or more) the same relation continued to exist. A comparable number in each group had the opposite condition, that is, hypocholesteremia (160 mg per hundred cubic centimeters or less). Operation had little effect on the general level of blood cholesterol. Only 40 per cent of the patients with stones showed a change of more than 10 per cent in the values for blood cholesterol, as against a 43 per cent incidence of such change in the group without stones. The values for blood cholesterol in an individual case may vary widely, but when mean results are determined for a group of cases they remain remarkably constant.

TABLE 2—*Blood Cholesterol of Patients Operated on for Disease of the Gallbladder (239 Patients)*

	Calculous	Noncalculous
Average value for blood cholesterol on admission to clinic	207 mg /100 cc	204 mg /100 cc
Average value for blood cholesterol immediately before operation	204 mg /100 cc	200 mg /100 cc
Average value for blood cholesterol 1 to 6 months after operation	206 mg /100 cc	206 mg /100 cc
Percentage showing hypercholesteremia preoperatively (220 mg /100 cc or more)	29	29
Percentage showing hypercholesteremia postoperatively (200 mg /100 cc or more)	31	34
Percentage showing no change (less than 10 mg /100 cc) in postoperative period	60	57

Roentgen Study—A cholecystogram of each patient was made by the Graham-Cole technic. The diagnosis of stones was accurate in cases in which the gallbladder was visualized. Since the use of the double dye method of visualization an accurate roentgen diagnosis has been made in 95 per cent of cases of stone in which the gallbladder concentrates dye. Gallbladders that fail to visualize by the double dye method are gallbladders with obliterated lumens and containing stones or gallbladders with intermittent complete obstruction (hydrops) of the cystic duct.

During the past nine years approximately 2,600 patients have been examined and followed in the clinic for patients with disease of the gallbladder without the known development of stones in any who did not have them on admission to the clinic. Twiss and Barnhard⁷⁷ concluded that this was due to the control of stasis by therapeutic means and to the dietary control of the cholesterol intake.

Operative Material—At operation the gallbladder was removed and specimens of bile were obtained for chemical, microscopic and bacteriologic examination. (The incidence of the various pathologic types of bile is given in table 3.) Cultures were made of the remaining bile or material from the wall of the gallbladder.

77 Twiss I R and Barnhard J H. Disease of Biliary Tract Associated with Disturbances in Cholesterol Metabolism. *J A M A* **111** 990 (Sept 10) 1938.
Twiss I R and Greene C H. Dietary and Medical Management of Diseases of the Gall Bladder. *ibid* **101** 1841 (Dec 9) 1935.

of material from the cystic lymph node and of the common duct bile. A culture of any of these which yielded bacteria was considered evidence of viable organisms in the gallbladder. The results of the cultures for the various types of disease of the gallbladder encountered are given in table 4.

It is evident that gallbladders which showed a normal concentration of dye on preoperative roentgen examination rarely showed organisms either in their bile or in the wall. Furthermore, only 38 per cent of these gallbladders with stones showed evidence on microscopic examination of previous mucosal inflammation or infection.

The values for bile salts and bile acids in the gallbladders were determined by both the Reinhold-Wilson⁷⁸ and the Aldrich-Bledsoe⁷⁹ methods. These are both colorimetric methods, and their use has been challenged because of nonspecificity

TABLE 3—*Pathologic Classification of Gallbladders Removed*

Specimens normal or showing evidence of dysfunction without stones	23
Specimens showing chronic cholecystitis without stones	11
Total noncalculous gallbladders	40
Specimens showing evidence of metabolic disturbance or dysfunction with stones	29
Specimens showing chronic cholecystitis with stones	109
Specimens showing acute cholecystitis	11
Total calculous gallbladders	109

TABLE 4—*Incidence of Cultures Yielding Bacteria (Gallbladder Removed at Operation)*

	Calculous Gallbladders Percentage	Noncalculous Gallbladders Percentage
Dyskinesia*	16	13
Chronic cholecystitis	40	21
Acute cholecystitis	83	

* "Dyskinesia" represents the condition of gallbladders with a relatively normal pathologic picture and a normal concentration of the dye in preoperative roentgen examination.

and the effect of possible interfering substances in the bile. They do not distinguish between conjugated and free bile acids and do not show the presence of desoxycholic or other bile acids or their derivatives which do not contain the cholic acid group. The results (table 5), however, are of interest from the comparative standpoint. The results show wide fluctuations but indicate that the functioning gallbladder in general produces a greater concentration of bile salts than does a nonfunctioning gallbladder. The greatest concentration was found in the presence of stasis. The inflamed, thickened, infected gallbladder either failed to concentrate bile salts or absorbed them.

The cholesterol content of gallbladder bile also varied to a great degree. Table 6 is a study on cholesterol content similar to the one on bile salts. Determination

78 Reinhold, J. G., and Wilson, D. W. The Determination of Cholesterol in Bile, *J. Biol. Chem.* **96** 637 (June) 1932.

79 Aldrich, M., and Bledsoe, M. S. Studies in the Metabolism of Fats. I. A Quantitative Pettenkofer Test Applicable to the Determination of Fats in Blood, *J. Biol. Chem.* **77** 519 (May) 1928.

of the cholesterol content were performed according to the method of Lieboff⁵⁰ It was noted that as the severity of the pathologic changes found at operation increased the cholesterol content of the gallbladders decreased. In calculous gallbladders that were functioning, i. e., that concentrated and emptied the dye on roentgen examination, the cholesterol content was much higher than in those shown by the roentgen rays to be nonfunctioning. This is interpreted as indirect evidence

TABLE 5—*Bile Salt Content of Calculous and Noncalculous Gallbladders*

	Average Bile Salt Concentration Mg /100 Cc	Percentage 25% Below Mean Average	Percentage 25% Above Mean Average
Noncalculous gallbladders			
Dyskinesia and chronic cholecystitis	3.154 ± 300	40	21
Calculous gallbladders	3.910 ± 300	35	16
(a) Dyskinesia	4.780 ± 150	14	7.6
(b) Chronic cholecystitis	3.745 ± 400	44	20
(c) Obliterative cholecystitis	1.785 ± 360	62	12

TABLE 6—*Cholesterol Content of Calculous and Noncalculous Gallbladders*

	Average Concentration Mg /100 Cc	Percentage with Concentration 25% Below Mean Average	Percentage with Concentration 25% Above Mean Average
Noncalculous gallbladders			
Dyskinesia and chronic cholecystitis	475 ± 60	22	23
Calculous gallbladders	573 ± 125	22	32
(a) Dyskinesia	720 ± 130	15	28
(b) Chronic cholecystitis	540 ± 140	25	22
(c) Obliterative cholecystitis	253 ± 30	12	50

TABLE 7—*Bile Salt-Cholesterol Ratio in Calculous and Noncalculous Gallbladders*

	Percent age with Ratio Le than 18:1	Percent age with Ratio More than 18:1	Average Ratio
Noncalculous gallbladders			
Dyskinesia and chronic cholecystitis	80	20	7.7:1
Calculous gallbladders	86	14	7.5:1
(a) Dyskinesia	92	8	6.5:1
(b) Chronic cholecystitis	80	20	9.7:1
(c) Obliterative cholecystitis	88	12	8.7:1

of the concentrating power of the normal gallbladder for cholesterol. Another interpretation is that advanced by Elman and Graham⁵¹ who stated the belief that the normal gallbladder secretes cholesterol and that this function is impaired when the gallbladder is damaged.

The bile salt-cholesterol ratios in the different types of cases are given in table 7. In the majority of cases, whether or not stones were present, the ratio was below the level at which precipitation usually is assumed to occur. The analytic method

⁵⁰ Lieboff, S. I. A Simplified Method for Cholesterol Determination in Blood. *J. Biol. Chem.* **61**: 177, 1924.

used for determining the value for bile salts affects the absolute values obtained, so that these ratios are not strictly comparable with many others reported in the literature. It is significant that the ratio was low for as many patients without stones as with stones.

The significance of pancreatic ferments in the gallbladder bile has been variously interpreted. In this series of noncalculous gallbladders the pancreatic ferments were found in 53 per cent of all gallbladders and in 59 per cent of calculous gallbladders. The Myers and Fine⁸¹ methods of determination of the presence of ferment were used, and in each instance two or three ferments were considered necessary to indicate "positive" results. This stand was taken to obviate the misinterpretation of the finding of amylase in the gallbladder, as this ferment may be found in tissues totally dissociated from the pancreas.

Microscopic examination of the gallbladder bile revealed no significant variation between the calculous and the noncalculous gallbladders. In gallbladders with

TABLE 8—Summary of a Study of 100 Consecutive Gallbladders Removed at Operation with Complete Preoperative Work-Up and Meticulous Postoperative Examination

	Average Age of Patients, Yr	Average Duration of Symptoms, Yr	Average Bile Salt Concentration, Mg/100 Cc	Average Cholesterol Content, Mg/100 Cc	Bile Salt-Cholesterol Ratio			Percentage of Cultures Yielding Bacteria	Percentage with Microscopic Evidence of Previous Infection	Percentage with Hypercholesteremia	Percentage with Evidence of Damage to Liver	Percentage with Pancreatic Ferments
					Percentage Less than 18:1	Percentage More than 18:1	Average Ratio					
Noncalculous gallbladders	39	6	3,154	475	80	20	7.7:1	13	26	20	40	32
Calculous gallbladders (total)	40.6	7	3,910	573	86	14	7.5:1	34	78	29	16	60
(a) Dyskinesia	37	5	4,780	720	92	8	6.2:1	11	38	33	13	43
(b) Chronic cholecystitis	41	5.5	3,745	540	80	20	9.7:1	33	100	30	25	61
(c) Obstructive cholecystitis as shown by roentgen examination	51	12	1,785	253	88	12	8.7:1	100	100	12	0	30

acute inflammation (generally those with stones), pus, epithelial debris and mucus were found. Crystals in the gallbladder bile were present in 94 per cent of calculous gallbladders and in 73 per cent of noncalculous gallbladders. Microscopic examination of the stones gave no noteworthy information except that the gallbladders with a single cholesterol stone usually showed no evidence of previous inflammation and that material from them was sterile on culture in nearly every instance.

A summary of the possible causes for the gallstones found in our series is given in table 8. The incidence of these factors in calculous cholecystitis is in contrast to their incidence in noncalculous gallbladders. The factors summarized are (1) the age of the patients, (2) the duration of the active symptoms, (3) the bile salt concentration, (4) the cholesterol content, (5) the bile salt-cholesterol ratio, (6) the organisms on culture, (7) the evidence of a previous infection.

81 Myers, V. C., and Fine, M. S. A Consideration of the Chemical Methods Employed in Medical Diagnosis, *Post-Grad M. J.* 28:384, 1917. *Myers and Fine, Animal Diastases*, *J. Biol. Chem.* 29:179 (March) 1917.

(8) the presence of hypercholesteremia during the preoperative period of study, (9) evidence of hepatic damage and (10) the presence in the gallbladder of pancreatic ferments

COMMENT

Before discussing the application of specific theories to the cause of the stones found in our series, it is well to call attention to the patients' ages and the duration of active symptoms. These factors were nearly equal in the calculous and the noncalculous groups and therefore seem to have no bearing on the problem. The variation in action of such factors as were found to be equally prevalent in both groups cannot be attributed to a short interval during which they had been acting. The factors of age and duration of symptoms were significant only in gallbladders whose lumens were obliterated. This is what may be anticipated in cases of severe long-standing disease.

In this series of cases the level of blood cholesterol apparently did not play a role in the causation of stones. There is no way of determining what this factor may have been at the time the stones were first formed, but it was evident that an appreciable variation from normal did not persist, furthermore, the preoperative and postoperative levels of blood cholesterol were remarkably equal in the series as a whole. We found the same wide variations in the values for blood cholesterol that have always been an unexplained factor in such studies (Riegel, Ravdin and Rose¹²). During the period of study, there was nearly as high an incidence of hypercholesteremia in patients without as in those with stones (20 per cent and 29 per cent respectively). Moreover the general level of blood cholesterol as seen in our operative patients was that seen generally in our clinic on routine examination of the blood of patients without stones or organic disease of the gallbladder. It was slightly higher than that given in similar reports in the literature. Von Babarczy,⁶⁸ Twiss and Barnard,⁶⁹ Moynihan,⁴ Whitaker,²³ Dewey,⁶ and McMaster⁸² have stated the belief that the level of blood cholesterol can be controlled by diet and that dietary control may reduce the incidence of stones. It was noted that patients with hypercholesteremia who were observed for a time on a low cholesterol diet showed an appreciable reduction in the level of blood cholesterol. Because of the wide fluctuation of values for blood cholesterol in the same patient (Walsh,⁶ Dostal and Andrews,⁶⁶ Fox⁸³) and the general results in this series of cases we do not believe that the general level of blood cholesterol is materially influenced by the diet except over long periods. The fact, furthermore, that the average value for blood cholesterol was

82 McMaster P. D. Studies on Total Bile. Influence of Diet upon the Output of Cholesterol in Bile. *J. Exper. Med.* **40**: 25 (July) 1924.

83 Fox F. W. The Composition of Human Bile and Its Bearing upon Sterol Metabolism. *Quart. J. Med.* **21**: 107 (Oct.) 1927.

the same for the noncalculous patients as for those with stones confirms this belief and also the observations of Campbell⁸⁴. It was particularly evident in this investigation that a study of the blood at the time of operation is futile in arriving at a solution of the possible cause of the stones found in the gallbladder.

It has been mentioned that hepatic damage causes a change in the character of the bile which possibly may favor the formation of gallstones. A careful study of hepatic function preoperatively and a study of the liver by observation and biopsy at the time of operation have shown that nearly 40 per cent of noncalculous patients had some evidence of damage to the liver, as against only 16 per cent of calculous patients. No conclusion may be drawn from this finding except that the value of such functional studies in determining the cause of the gallstones is minimal. It must not be assumed from these findings that hepatic disease generally is more frequent in noncalculous than in calculous disease of the gallbladder, for in many instances a cholecystectomy was performed because of evidence of hepatic disease which was thought to be associated with chronic cholecystitis. This practice has been discontinued in the clinic during recent years.

A comparison of the chemical composition of bile from noncalculous with that of bile from calculous gallbladders does not justify the belief that a decrease in the bile salt-cholesterol ratio favors the formation of gallstones. In only 20 per cent of the noncalculous gallbladders did the ratios exceed 18:1, and in only 26 per cent did it exceed 13:1. In nearly 80 per cent of all noncalculous gallbladders the concentration of bile salts in the bile was below that ordinarily considered necessary to keep cholesterol in solution, and yet stones were not formed. Among the cases of calculus the ratios in 14 per cent were sufficient to keep cholesterol in solution, i. e. more than 18:1, and in 22 per cent the ratios were above 13:1. On this theory we found the average ratio in cases in which no stones were present to be 7.7:1, and that of cases in which stones were present, 7.5:1. It is evident that while bile salts may help to keep cholesterol in solution, changes in this purely chemical factor cannot be held accountable for the stones seen in this series of cases.

In this series there was a very low incidence of infection in noncalculous functioning gallbladders. In addition, only 1 in 4 gallbladders showed any pathologic evidence of a previous inflammation. The same low incidence of both findings was seen in the calculous gallbladders with normal function as shown by the roentgen rays. This contradicts the theory of Albeaux-Fernet⁸⁵ that transient infections, causing changes in the wall of the gallbladder but completely subsiding, are the cause of gallstones found in functioning gallbladders. The stones found in

⁸⁴ Campbell, J. M. H. Cholesterol in Blood in Cases of Gall Stones. *J. Med.* 18:123 (Oct.) 1924.

functioning gallbladders in this series frequently were cholesterol stones, but 60 per cent of all the stones in such gallbladders were "mixed" stones of the type usually ascribed to inflammation. The incidence of cultures yielding bacteria and of inflammatory evidence increased with the severity of the general process. Cultures of material from gallbladders with obliterated lumens yielded bacteria in nearly every instance. Differences in the proportionate number of such cases in the series perhaps accounts for the low incidence of infection in this series of cases as compared with the results reported by earlier investigators. From these findings it appears reasonable to assume that in many instances the stones preceded the infection, their presence acting as an irritant and so providing a means for the entry of bacteria into the wall of the gallbladder. Only 33 per cent of patients with "early cholecystitis" with or without stones showed either bacteriologic or pathologic evidence of previous or present inflammation or infection.

Stasis was a finding common to almost all the gallbladders in this series. Stasis was diagnosed preoperatively by the finding of a dense concentration of the dye in the cholecystogram by a delay in evacuation after a fatty meal and by the obtaining of concentrated bile with crystalline sediment on duodenal drainage. At operation this was generally confirmed by finding crystals in the gallbladder bile. This would seem a strong argument for stasis as a cause of gallstones were it not that the incidence of stasis as here defined was as great in the noncalculous gallbladders as in those with stones. As nearly as could be determined from the symptoms stasis had been present for as long a period in the one type as in the other. Bile stasis was the one factor present in cases with stones that did not show evidence of past or continuing infection. In gallbladders with impaired visualization on roentgen examination and with evidence of a past or continuing infection, crystals and other evidence of stasis were invariably present. It could not of course be determined which was the primary condition.

The results of our study on pancreatic ferments in operative gallbladders were interesting but inconclusive. This possible factor in the formation of gallstones has received little attention in the literature. It merits a further study, for the anatomic relation existing between Wirsung's duct, the common duct and the ampulla of Vater allows pancreatic reflux into the gallbladder to take place in many patients. It is here that spasm of the sphincter may play a role in producing not only stasis in the biliary tract but pancreatic reflux. In this series such a reflux was suggested by the finding of pancreatic ferments in the bile at operation in 53 per cent of the noncalculous gallbladders and in 59 per cent of those with calculi. A further study on pancreatic reflux especially when correlated with a deficiency of fatty acids and saponifiable substances is desirable.

SUMMARY

The study of this series of cases has served to emphasize the difficulty of determining the cause and pathogenesis of gallstones solely by a study of the patient at the time of operation. If the deposition of a calculus depends on the concomitant action of several different factors, the period of calculus formation may be limited, and a study of the patient one to twenty-five years later will fail to present the true picture of the conditions determining the deposition of the stone. It must also be recognized that the different types of gallstones may have different causes. When the various factors theoretically advanced as causes of gallstones are studied and correlated, no single factor or combination of factors satisfactorily explains the stones found in this series of cases.

The findings in this study furnish presumptive evidence that the composition of either the hepatic bile or of that obtained by duodenal drainage is not related to the changes in the chemical composition of the blood and that the cholesterol content of the gallbladder as determined at operation is not related to cholesterol content of the blood. Furthermore, this study has shown that the bile salt-cholesterol ratio is widely variable in all types of pathologic changes of the gallbladder and is often very low even in noncalculous gallbladders, that hypercholesteremia as determined by preoperative studies of the blood is not related to the presence of stones, and that pancreatic ferments are as common in noncalculous gallbladders as in those with calculi.

We were unable to show that there was any difference in the incidence of stasis in the cases in which gallstones were present and in the cases in which there were no stones. In 25 per cent of cases in which gallstones were present, stasis was the only one of the factors considered in the pathogenesis of stones which could be demonstrated. There is a strong presumption, therefore, that stasis was of importance in the formation of gallstones, but other, unknown factors must also have been in operation, for 86 per cent of the noncalculous gallbladders also showed evidence of stasis.

In 24 cases there were gallstones unassociated with any bacteriologic or pathologic evidence of infection or inflammation. This group of cases is evidence that infection is not necessary to the formation of stones and presumptive evidence that in many cases stone-precipitation without infection of the gallbladder.

TREATMENT OF VARICOSE VEINS

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Recent advances in the knowledge of varicose veins have emphasized the importance of three factors, namely, careful diagnosis, proper selection of cases and adequate therapeutic procedures. A systematized method of evaluating, selecting and treating the patients is therefore essential. At the University Hospitals the following concepts have proved valuable in relieving the greatest number of patients with varicose veins.

ANATOMIC CONSIDERATIONS

The usual anatomic positions of the venous components in the lower extremity are illustrated in the accompanying diagram¹. The deep veins are the anterior tibial, posterior tibial, peroneal, popliteal and femoral. The superficial veins are the long saphenous and the short saphenous with their many tributaries, including the accessory branches entering the saphenous fossa. The communicating veins connect the superficial and the deep veins. There are usually one to three communicating veins in the thigh and as many as fifteen to thirty in the leg². Blood normally flows upward through the superficial and deep veins. The superficial veins empty their blood into the deep veins at the junction of the long saphenous vein with the femoral vein, at the junction of the short saphenous vein with the popliteal vein and through the various communicating veins. Under normal conditions venous valves prevent a reflux of blood when the patient is in the upright position.

PATHOLOGIC PICTURE

Dilatation of superficial veins may be due to one or more of the following factors: congenital weakness of the venous walls or valves, obstruction of the deep veins, thrombophlebitis, pregnancy, trauma, tight clothing and prolonged standing. Whenever the varicose state develops, the venous valves become incompetent and a reflux of blood occurs.

From the Department of Surgery, the University of Iowa College of Medicine.

1. Edwards, E. A. The Treatment of Varicose Veins. Anatomical Factors of Inflation of the Great Saphenous Vein. *Surg., Gynec. & Obst.* **59**: 916-928 (Dec.) 1934.

2. Linton, R. R. The Communicating Veins of the Lower Leg and the Operative Technique for Their Ligation. *Ann. Surg.* **107**: 583-593 (April) 1938.

Patients with varicose veins have been classified for diagnostic and therapeutic purposes according to the location of the venous insufficiency, as follows

Group I Patients with deep venous obstruction with compensatory dilatation of any or all of the superficial veins

Group II Patients with incompetence of the valves in a dilated long saphenous vein

Group III Patients with incompetence of the valves in the dilated long saphenous vein and in the communicating veins of the thigh

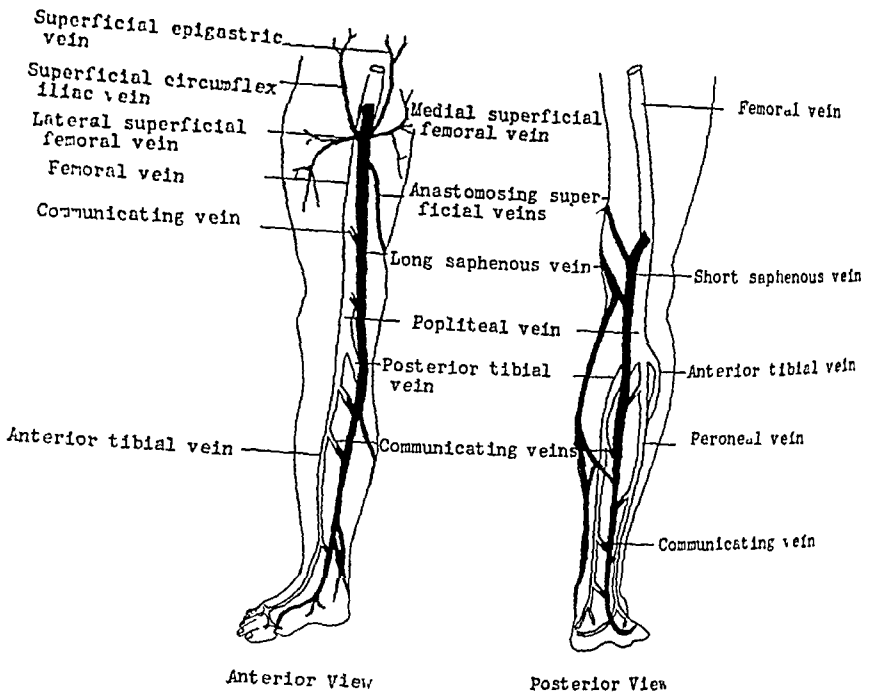


Diagram of the venous components in the lower extremity

Group IV Patients with incompetence of the valves in the dilated long saphenous vein and in the communicating veins of the leg

Group V Patients with incompetence of the valves in the dilated communicating veins of the thigh with involvement of the long saphenous vein below the femorosaphenous junction but with no reflux of blood through the femorosaphenous junction

Group VI Patients with incompetence of the valves in the dilated communicating veins of the thigh without involvement of the long saphenous vein

Group VII Patients with incompetence of the valves of the dilated long saphenous vein with secondary dilatation of the short saphenous vein below the popliteosaphenous junction but with no reflux of blood from the popliteal to the short saphenous vein

Group VIII Patients with incompetence of the valves in only the dilated short saphenous vein

Group IX Patients with incompetence of the valves in both the long and the short saphenous veins with a reflux of blood through the femorosaphenous and the popliteosaphenous junction respectively

Group X Patients with incompetence of the valves in the dilated communicating veins of the leg

Group XI Patients with incompetence of the superficial venous walls with simple dilatation but no incompetence of the valves in any of the veins

EXAMINATION AND DIAGNOSTIC TESTS

The examination of the patient must reveal in which of the aforementioned groups he can be placed. Various diagnostic procedures are used for identifying the dilated veins, for evaluating the patency of the deep veins and for locating the incompetent valves or "blow-out points."

Inspection of the extremities with the patient standing in a good light will usually reveal the size and distribution of the varices. Dilatations directly related to the long saphenous vein are located on the medial aspect of the thigh and leg, however, much anatomic variation is noted with different patients. Varices related to an incompetent short saphenous vein are found on the posterolateral surface of the leg. Varices which appear to originate on the lateral aspect of the thigh and leg are often associated with obstruction of the deep veins.

The Schwartz test, which is performed by palpating the long or the short saphenous vein with one hand while percussing the varicose veins with the other hand, often reveals the relation of these trunks. This test will aid also in determining the presence and location of a dilated long saphenous trunk in the thigh of an obese patient.

The Perthes test was designed to give information concerning the patency of the deep veins. This test is performed by placing a tourniquet around the extremity above the varices and observing the condition of the varices as the patient walks. If they become more prominent, the deep veins are obstructed. Such a result from a Perthes test is considered positive. If, however, the varices collapse or become less prominent the deep veins are patent and the result of the test is negative. Sometimes two tourniquets, one above and one below the varices, give added information. Tourniquets may be placed at different levels along the extremity if necessary. The latter procedure, which is often more efficacious than the simple Perthes test, is called the segmental Perthes test.

The Trendelenburg test aids in locating the incompetent valves. It is performed by elevating the extremity until the varices collapse and then observing the rapidity of filling when the patient stands with a tourniquet

constricting the upper end of the long saphenous vein. The rapidity of filling when the obstructing tourniquet is suddenly removed is also noted. If the varices remain empty or fill slowly with the tourniquet in place and then fill rapidly when the tourniquet is removed, the varicose condition is due to incompetence of the valves in the long saphenous vein. The aforementioned results are classified as singularly positive and include groups 2 and 7.

If the varices fill rapidly with the tourniquet still in place, there is also incompetence of the valves in the communicating veins of the thigh or leg. If additional bulging of the veins is observed when the tourniquet is removed, the valves at the junction of the saphenous with the deep vein are also incompetent. If no additional bulging is noted when the tourniquet is removed, the incompetent valves are in the communicating veins only. The results are classified as doubly positive whenever the varices fill immediately or in less than thirty seconds with the constricting tourniquet still in place. A doubly positive Trendelenburg reaction therefore is obtained in patients of groups III, IV, V, VI and X.

A negative result from a Trendelenburg test indicates that the varices fill slowly from below whether the tourniquet is still in place or not.³ In this condition no reflux of blood occurs through the saphenous or communicating veins, because the varicose state is due to incompetence of the venous walls and not to valvular insufficiency. In patients of group XI the result of the Trendelenburg test is negative.

If the valves in both the long and the short saphenous vein are incompetent, the examiner must repeat the Trendelenburg test, using two tourniquets, one being placed around the upper part of the thigh and the other just below the knee to constrict the long and the short saphenous vein respectively. The patients in group IX require the use of two tourniquets.

Incompetence of the valves in the short saphenous vein alone may be diagnosed by applying the tourniquet around the leg, just below the knee. The interpretation of the test is similar to that for the long saphenous vein. A singularly positive result from the Trendelenburg test with the tourniquet below the knee indicates that the varices are related to an incompetent short saphenous vein (group VIII). A doubly positive result with the tourniquet below the knee indicates that the incompetent valves are in the communicating veins of the leg (group X).

3 The three interpretations of the Trendelenburg test given here are the most commonly used. Bernstein defined four possible results: positive, double, and nil (Bernstein, A., in McPheeters, H. O. *Varicose Veins with Special Reference to the Injection Treatment*, ed 2, Philadelphia, F. A. Davis Co., 1930, p. 43). His interpretations, however, are more complicated and less used.

The comparative tourniquet⁴ test is a refined development of the segmental Perthes test, and it may reveal all the information obtainable by both the Perthes and the Trendelenburg test except the degree of incompetency of the valves. The comparative tourniquet test is performed by observing the size of the varices under five (sometimes six) different conditions: (1) with the patient standing, (2) with the patient walking, (3) with the patient walking with a tourniquet around the upper part of the thigh, (4) with the patient walking with a tourniquet around the middle of the thigh, and (5) with the patient walking with a tourniquet around the lower part of the thigh. Occasionally it will be necessary also to observe the varices with the tourniquet around the leg just below the knee. The interpretation is as follows:

1 The deep veins are patent if the varices diminish when the patient walks with or without the tourniquet in place anywhere along the extremity.

2 The deep veins are not patent if the varices increase in prominence during any or all of the walking procedures.

3 The long saphenous valves are insufficient if the improvement in the varices is the same with the tourniquet around the upper part of the thigh as with the tourniquet around the lower part of the thigh.

4 The valves of the communicating veins in the thigh are incompetent also if the improvement is greater with the tourniquet around the lower or the middle part of the thigh than with the tourniquet around the upper part of the thigh. The location of the incompetent vein or veins can be determined by comparing the degree of improvement at each of the three levels in the thigh.

5 If the varices do not improve with the tourniquet around the lower part of the thigh, one or more of the following conditions exist. The valves in the short saphenous vein are incompetent, the valves in the communicating veins of the leg are incompetent or the deep veins are not patent. In order to distinguish between these three conditions the tourniquet is placed below the knee, constricting the upper end of the short saphenous vein. If the varices are now observed to collapse on walking, the reflux of blood is coming through incompetent valves in the short saphenous vein. If the communicating veins of the leg are insufficient, the varices will remain the same size as when the patient walked with the tourniquet around the lower part of the thigh. If the deep circulation is not patent the varices will become more prominent on walking.

⁴ Mahorner, H. R., and Ochsner, A. O. The Modern Treatment of Varicose Veins as Indicated by the Comparative Tourniquet Test. *Ann. Surg.* **107**: 927-950 (June) 1938.

the metacarpophalangeal joint of the third, fourth and fifth fingers was noted. The wrists and the terminal phalanges were hyperextensible. The four lateral toes of each foot were contracted by a cutaneous web (fig 9A). A lateral roentgenogram of the skull (fig 9B) showed the sella and the general architecture of the skull to be normal.

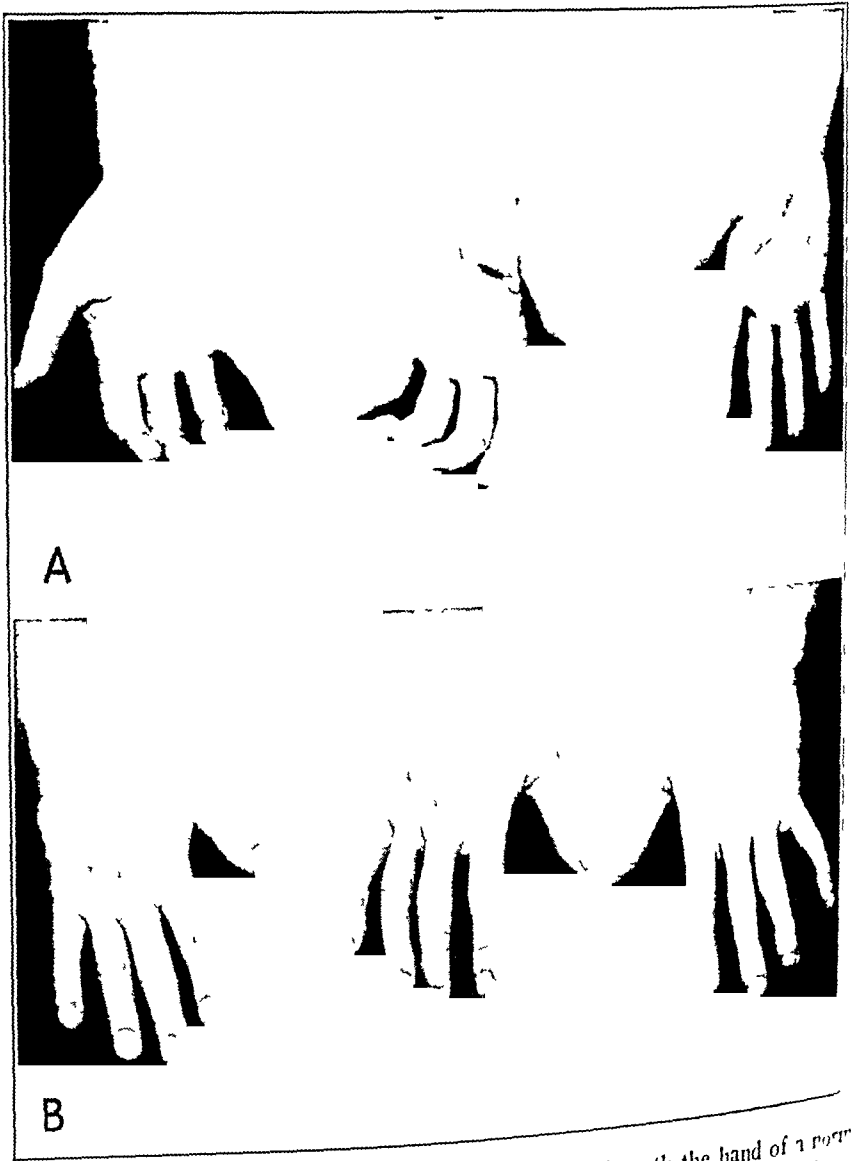


Fig 11 (case 4) —Comparison of the patient's hands with the hand of a normal person. A, palmar aspect, B, dorsal aspect. Note the contractures of the fingers.

CASE 4—M. T. (fig 10A), a man aged 45, was seen because of pain in the suboccipital region, loss of memory and spots before the eyes. Four years prior to admission he noticed floating spots before his eyes. Examination at that time revealed hemorrhages into the right retina. Shortly after this, vision became defective on that side. He had had intermittent pain which radiated from the frontal to the occipital region. Contractures of the fingers and toes had been present since birth. Constant stretching improved the deformities of the fingers.

In childhood it was possible to dislocate the patellas at will. No dislocation had occurred in the last few years, and it appeared that the patellas had become more stable. The feet were long, a size 12 shoe being required. His father, his paternal grandfather, a sister and her two daughters, who were half-sisters, had similar deformities (fig 12). One sister was living and had no abnormalities.

Examination—The patient weighed 184 pounds (83.5 Kg). The head was of normal shape. The cornea of the right eye was clear. The media were cloudy, and the iris appeared dull. The anterior chamber was shallow, owing to



Fig 12 (case 4)—Family of the patient. *A*, paternal grandfather, *B*, father, *C*, brother, *D*, sister. All have long, thin, contracted fingers and slipping patellas. *E*, daughters of *D*, one aged 16 years, with contracted fingers and slipping patella, the other aged 6 years, with no deformities. *F*, half-sister of patients in *E* and daughter of *D*. Note the long fingers with contractures. *G*, elder sister (*E*) in infancy. *H*, the earliest photograph of the patient.

bulging forward of the iris. The lens was moderately opaque. The disk was not seen. The pupil was contracted and fixed. The tension of the right eye was 13 and that of the left 19 (Schiotz-Gradle). A diagnosis of uveitis peracta of the right eye was made and enucleation was performed. The ears were normal. The palatal arch was not high. The teeth were normal. Except for a mild dorsum rotundum no deformity of the spine was noted. The hips were wide and the adipo-

tissue increased. The extremities distal to the elbows and knees appeared long and thin. The fingers were contracted at the metacarpophalangeal and interphalangeal joints. The thumbs were not affected, and the index finger was affected to a slighter degree than the remaining ones. The contractures were most marked at the proximal interphalangeal joints, the third and fourth fingers having the most marked deformity. These two fingers were contracted nearly 45 degrees at

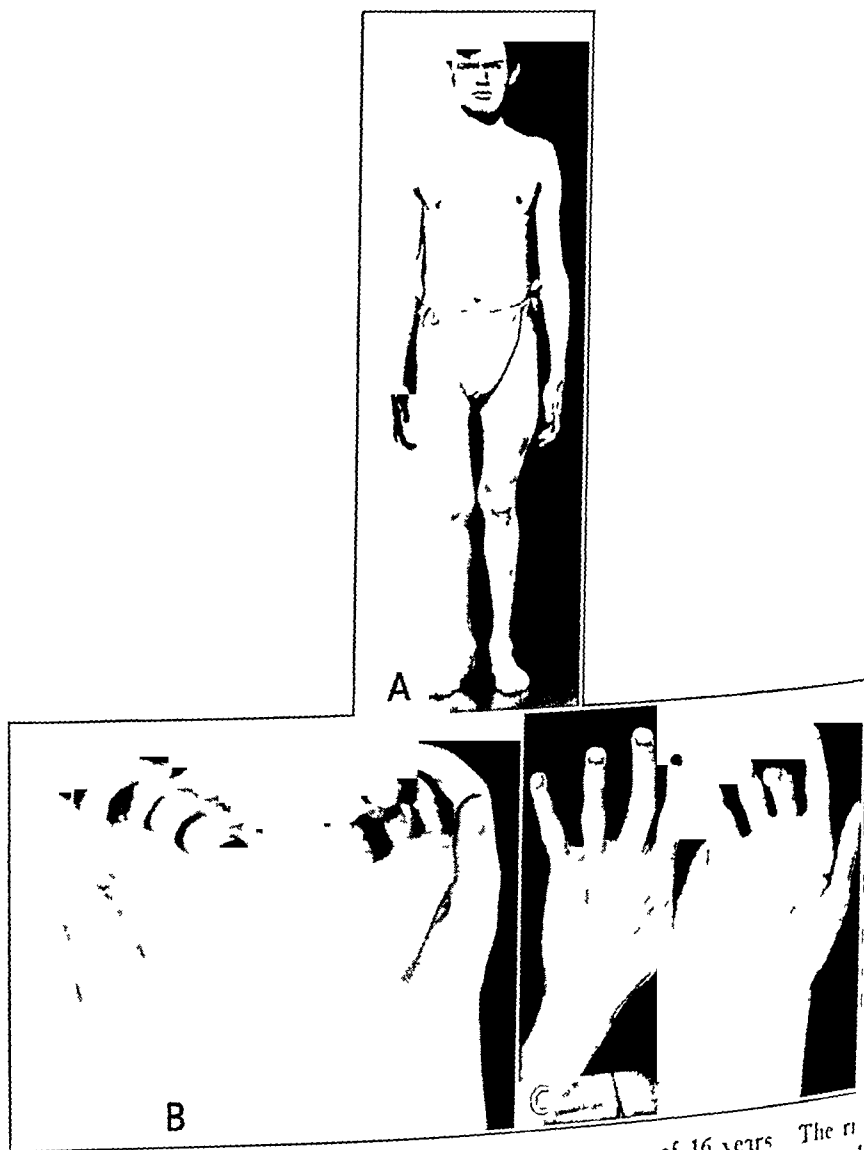


Fig 13 (case 5)—*A*, photograph of R. G. at the age of 16 years. The right patella is abnormally high, and there is wasting of the vastus medialis muscle more pronounced on the right. *B*, appearance of the hands at the age of 14 years with the fingers in maximum extension. *C*, improvement in contracture of the fingers following treatment. The contracture is most marked in the middle finger

this joint. The metacarpophalangeal and the distal interphalangeal joint show only slight contracture. Flexion of the terminal phalanges was limited. The little finger of each hand was curved toward the ring finger (Fig. 11). The soft tissue of the extremities was considerably reduced. The lower

of the vastus medialis muscle on both sides was poorly developed. The patellar ligaments were long and relaxed. The patella was abnormally high on each femoral condyle and displaced laterally. The digits were not relatively increased in length. The toes were long and slender and were contracted to a slighter degree than the fingers. The first toe, like the thumb, was not contracted. Roentgenograms of the skull showed some abnormal calcification of undetermined nature adjacent to the pineal body. The sella and the general shape of the skull were normal. Microscopic examination of a piece of gastrocnemius muscle showed normal striated muscle. No increase in glycogen could be demonstrated by Best's carmine technic.⁶²

CASE 5—R. G. (fig. 13-4), a boy aged 14 years, was seen because of repeated displacement of the left patella. He was born at full term by instrumental delivery and weighed 9½ pounds (4,309 Gm.). He started to walk and to talk at the normal age. Dislocation of the patella first occurred at the age of 8 years and was spontaneously reduced. Contractures of the fingers and toes were noted by his parents at his birth. His intelligence was normal. The father had no deformi-

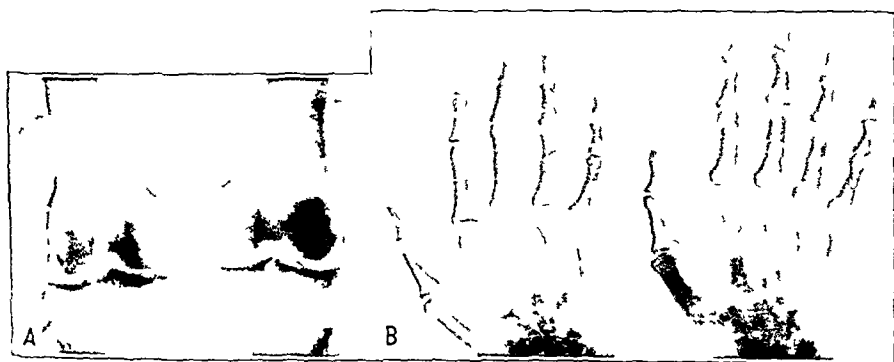


Fig. 14 (case 5)—A, roentgenogram of the knees showing bilateral dislocation of the patella and a prematurely closed epiphysis. B, roentgenogram of the hand (left) contrasted with the hand of a normal adult. Note the abnormally wide articular cartilage space of the metacarpophalangeal joints of the thumb and index fingers. The heads of the metacarpal bones are widely separated. The ring finger is the longest digit of the patient's hand.

ties. One sister 12 years of age was normal. His mother (fig. 15-4) and maternal grandmother had similar deformities.

Examination.—The patient weighed 118 pounds (53.5 Kg.) at the age of 16 years and was 66½ inches (169 cm.) tall. His head was of normal shape. The ears were large and the cartilaginous structures were poorly developed. The antitragus of each ear was enlarged. The eyes were normal. The chest was long with a narrow sternum and a mild pigeon breast deformity. There was a soft systolic murmur at the base of the heart. No curvatures or deformities of the spine were noted. The extremities were long and the subcutaneous tissue scanty. The fingers were contracted at the metacarpophalangeal and interphalangeal joints.

62. Kolmer J. A. and Boerner F. *Approved Laboratory Technique. Clinical Pathological, Bacteriological, Mycological, Parasitological, Serological, Biochemical and Histological*, ed. 2. New York: D. Appleton Century Company, 1938.

(fig 13 B) All the fingers were involved except the thumbs, the index fingers to a less degree than the medial three fingers. The interphalangeal joints of the ring and middle fingers showed the greatest degree of contracture. There were no contractures at the shoulders, elbows or wrists. The soft tissues of the extremities were scanty. Each vastus medialis muscle was underdeveloped in its lower portion. Both patellas were abnormally high and displaced outward on the lateral femoral condyles. The patellar tendons were long and relaxed, permitting the patellas to move abnormally high when the quadriceps femoris muscle contracted. The last 10 degrees of extension was done with difficulty because of the relaxed

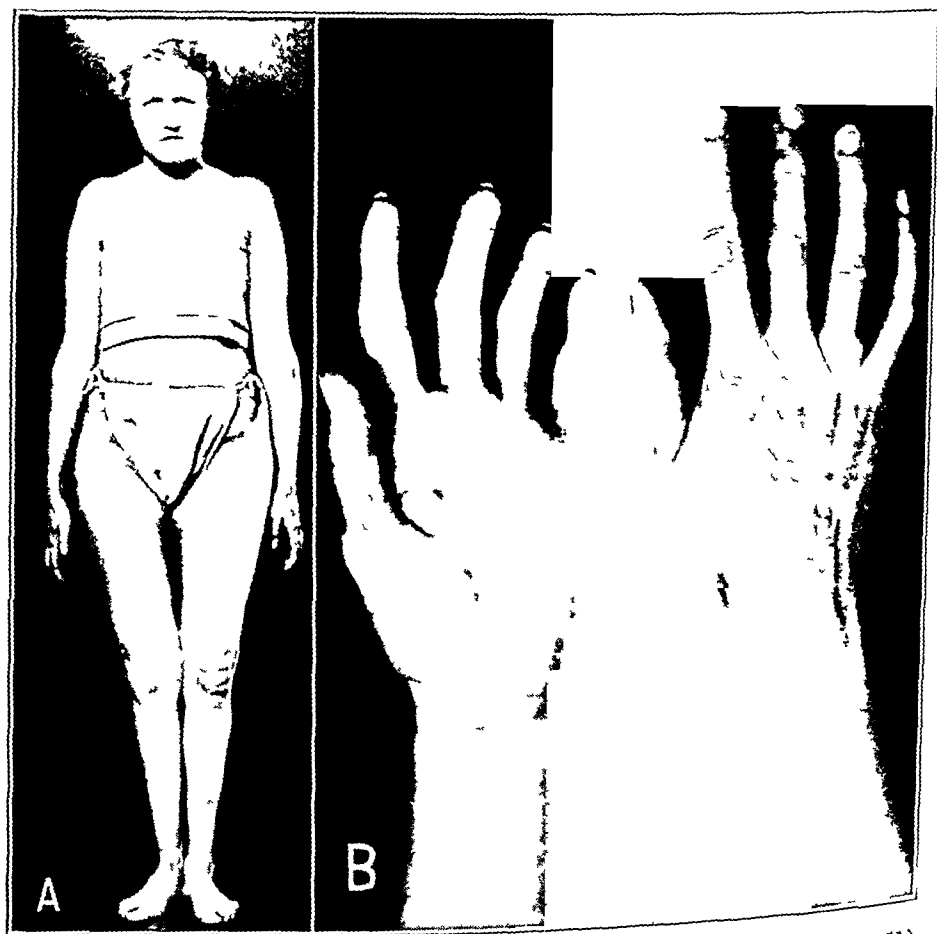


Fig 15 (case 6) —A, M G, a woman aged 36 years (mother of R G [case 5]) Note the long contracted fingers, the straight forehead and the soft tissue thinness of the extremities. B, photograph of the hands, showing contracture of the fingers, most marked in the fifth digit. The soft tissue of the fingers is small.

patellar tendons. There was mild contracture of the four lateral toes by shortness of the soft tissue. A Goldthwait operation was performed to correct the slipping patella on the left. At operation the patellar tendon was found to be about three times the normal length. The contracted fingers were improved by use of intermittent traction and passive stretching. A photograph (fig 13 C) taken at the age of 16 years, two years after the time when he was first seen, showed an improvement in the flexion contracture deformity of the fingers. A roentgenogram of the hand (fig 14 B) showed long, narrow metacarpal and phalangeal bones.

The fingers were slightly curved toward a line between the middle and ring fingers. The spaces between the heads of the metacarpal bones appeared to be abnormally wide. The articular cartilage space of the metacarpophalangeal joints of the thumb and index fingers was unusually wide. The fourth finger was the longest, whereas in the normal hand the third digit is the longest.

CASE 6—M G (fig 15 A), aged 36 years, mother of R G (case 5), had had recurrent dislocation of both patellas since the age of 11 years. Dislocations had at first occurred as many as four times a year, but had ceased during recent years. Contractures of the fingers and toes had been present as long as the patient could remember. There had been a gradual improvement in the finger deformities with constant stretching. The patient's mother had similar contractures of the fingers and toes. There has been no difficulty with vision.

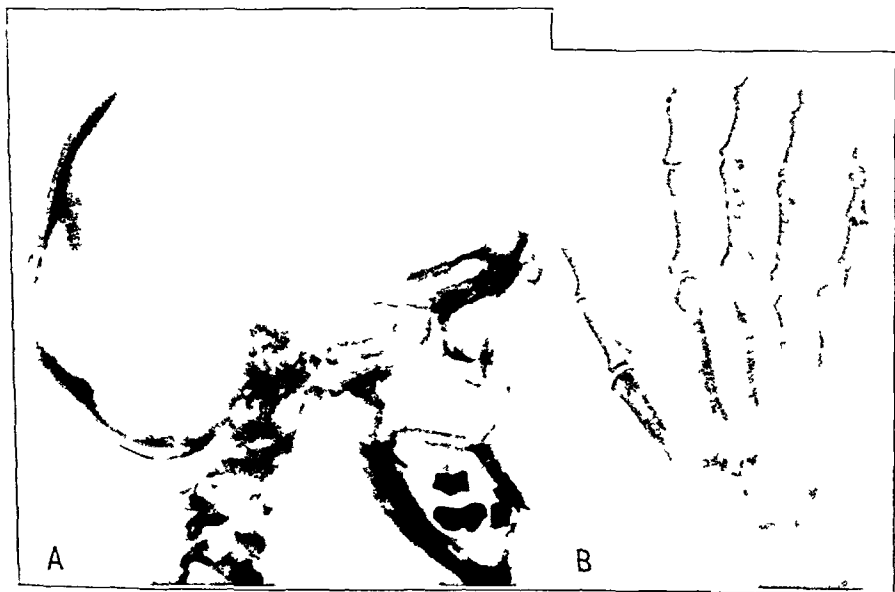


Fig 16 (case 6)—A, lateral roentgenogram of the skull of M G showing a moderate degree of prognathism. The sella is normal. B, roentgenogram of the right hand showing slender bones and scant soft parts. The articular cartilage space of the metacarpophalangeal joints of the thumb and index fingers is unusually wide. The fifth digit is curved inward.

Examination—The patient was 65.7 inches (162 cm) tall and weighed 128 pounds (58.1 Kg). The forehead was straight. There was a moderate degree of protrusion of the mandible. The cartilaginous structures of the ears were poorly developed. The eyes were normal. There was no spinal deformity. A pigeon breast deformity was present. The extremities were long and slender. The soft tissue about the hands was considerably reduced, exaggerating the length of the fingers. The patellas were displaced upward on the lateral femoral condyles and the patellar ligaments were elongated. The fingers, with the exception of the

thumb, were contracted at the metacarpophalangeal and interphalangeal joints (fig 15 *B*). The first phalanges could be extended to within 10 degrees of normal. The interphalangeal joints of each digit were equally contracted. The medial fingers showed the most pronounced contracture. While there was some decrease from the normal in the circumference of the legs and forearms, this was more evident about the digits. A roentgenogram of the hand (fig 16 *B*) showed slender bones and scantiness of the soft parts. The lateral curvature of the little finger and the medial curvature of the middle finger were exaggerated. The articular cartilage space of the metacarpophalangeal joints of the first and second fingers appeared unusually wide (fig 16 *B*). The hands and feet were not elongated out of proportion to the height. There was no contracture of the toes. A lateral roentgenogram of the skull showed mild prognathism and a normal sella turcica (fig 16 *A*).

ETIOLOGIC AND FAMILIAL ASPECTS

The cause of arachnodactyly is as obscure as that of other congenital abnormalities.

There is a family history connected with over half the reported cases. Weve⁴ reported 23 cases in six families and called particular attention to the familial tendency. Typical cases occur in families without a history of the disease on either side (cases 1, 2 and 3). Either sex may transmit the condition through three or four generations.

CHANGES IN SOFT TISSUE

In all cases there is a decrease of soft tissue in some portion of the body. Because of this decrease and wrinkling of the skin the face usually has an aged appearance. While soft tissue is fairly well preserved about the pelvis, it is considerably reduced in the extremities, particularly about the fingers and toes. The term muscle dystrophy has been used to describe the smallness of the soft tissues, but this term implies a wasting disease, such as primary muscular dystrophy.

That arachnodactyly may be a form of primary muscular dystrophy has been suggested. Spinal deformity, decrease of soft tissue and a familial tendency are common in both conditions. The difference between these syndromes, however, is more striking than their similarities. The apparent muscular atrophy in arachnodactyly is present at birth and is not progressive, and weakness is proportional to the size of the underdeveloped muscles. Microscopic examination of muscle from 2 patients (cases 1 and 4) showed normal muscle tissue.

Thursfield⁷ stated the opinion that the muscular involvement in arachnodactyly and that in amyotonia congenita are similar in some respects. In amyotonia congenita or Oppenheim's disease, however,

⁷ Thursfield, H. Arachnodactyly, *St Barth Hosp Rep* 53:35, 1917.

there is marked muscular atony without apparent muscular atrophy. The condition tends gradually to improve. Microscopic examination of muscle shows muscle fibers of normal size intermingled with many small fibers. The fibers retain their normal striated appearance.

LIGAMENTOUS RELAXATION AND CONTRACTURES

Some type of ligamentous relaxation is always present and is usually most pronounced in the joints of the hands and feet. In cases described by Patterson⁸ and by Burch⁹ there was marked relaxation of the sternoclavicular joint, with subluxation. The patellar ligaments are frequently elongated with the patellas located laterally and superiorly on the femoral condyles, making the last few degrees of extension difficult. There may be elongation and relaxation of the patellar ligaments without a history of dislocation. The patellar ligaments in 1 patient (case 5) were nearly three times as long as normal, and he had had repeated displacements. A roentgenogram revealed no abnormality of the femoral condyles. Two adult patients (cases 4 and 6) who had had recurrent dislocations in childhood had not observed recurrence for some years prior to observation. It seemed that stability in this region was increasing with advancement of age. Each of the 3 patients (cases 4, 5 and 6) who gave a history of dislocation of the patellas showed underdevelopment of the lower and medial portions of the vastus medialis muscle. When contractures occur, the fingers and toes are usually involved but occasionally only the larger joints are affected. A similar pattern of contracture about the hands was noted in cases 3, 4, 5 and 6. In none of these cases was any involvement of the thumb apparent, and the index finger was less affected than the other digits. In 3 cases (cases 4, 5 and 6) the metacarpophalangeal and interphalangeal joints were contracted and the palmar soft tissues shortened. In these cases the maximum contracture was found at the interphalangeal joints. In another case (case 3) the patient had contractures only at the metacarpophalangeal joints. In this case there was relaxation of the interphalangeal joints, resulting in hyperextension when the hand was opened. The interphalangeal joints of the middle finger of each hand in 1 patient (case 5 fig. 13) showed the most marked contracture. His mother (case 6 fig. 15 A) showed approximately the same degree of contracture of the interphalangeal joints of each finger, the contracture increasing from the index to the little finger of each hand. In case 4 the most

⁸ Patterson, W. I. Case of Arachnodactyly. *Canad. M. A. J.* 28: 652, 1933.

⁹ Burch, F. E. Association of Ectopia Lentis with Arachnodactyly. *Arch. Ophthalm.* 15: 645 (April) 1936.

prominent contracture occurred at the proximal interphalangeal joints of the third, fourth and fifth fingers. The little finger in cases 2, 4 and 6 was curved laterally. In 3 of the cases in which contracture of the finger was present there was some degree of contracture of the toes (cases 3, 4 and 5), the middle digit in each instance exhibiting the greatest deformity.

SKELETAL ANOMALIES

Persons with arachnodactyly are usually taller than normal persons and weigh less. The hands and feet are apparently or relatively lengthened. There was an apparent increased length of the fingers in all the cases reported here, with the exception of 1 case (case 5), because of decreased soft tissue. Measurements, however, indicated that there was no relative increase in length of the bones of the hands and feet as compared with other long bones. In 3 patients (cases 1, 2 and 4) an apparent increase in length of the toes was found.

Spinal deformity is commonly associated with arachnodactyly. In the 52 cases in which deformity was mentioned, scoliosis was present in 37, kyphoscoliosis in 8 and kyphosis in 7. The deformity usually appears in early life and is slowly progressive, but in most instances it does not become severe. It has been attributed to a poorly developed muscular system. Increased length of the spinal column may also be a factor. Moderate thoracic scoliosis was present in cases 1, 2 and 3. The onset in 1 patient (case 2) was noticed at 18 months, in another it was first observed at 4½ years (case 1). The curvature in 1 patient had its onset much later.

Deformities of the head are present in approximately 75 per cent of cases. Dolichocephalus, prognathism, narrow arched palate and asymmetry of the skull are among the common anomalies. Dolichocephalus was mentioned in 17 cases but could not be demonstrated by measurements in the cases reported here. In some instances the head is relatively increased in size, while in others it is smaller than normal, as was noted by Weill¹⁰. Roentgenograms of the skull in some cases have revealed prominence of the orbital roof with a corresponding shortening of the anterior cranial fossa. In 1 of the cases reported here this abnormality was noted (case 1). In 9 of the reported cases the sella was believed to be slightly reduced in size. In 9 cases there was protrusion of the chin. An example of this is illustrated in case 6. In cases 1, 2 and 3 the palate was high and narrow, and in 1 of these (case 3) it was curved to the right.

10 Weill, G. Ectopie des cristallins et malformations générales, *Ann. d'otol.* 169 21, 1932.

Deformities of the chest wall have been noted in nearly 50 per cent of the cases. A narrow flat chest, a funnel-shaped breast, projection of the lower part of the sternum and pigeon breast are some of the more common anomalies. A pronounced pigeon breast deformity was present in cases 3 and 6. The ears are frequently malformed. Enlargement of the lobes was the most frequent defect observed. In cases 1, 5 and 6 the lobes were large and flabby because of poorly developed cartilage. In some instances the crus helicis, antihelix and tragus are malformed.

HEART

Heart disease is a frequent accompaniment of the condition, about 35 per cent of patients showing some type of cardiac involvement. Piper and Irvine-Jones¹⁰ found mention of a cardiac disturbance in 8 of the 18 reported cases. In 5 of these it was believed to be on a congenital basis. A patent foramen ovale was found at autopsy in Borger's¹¹ case. A deficiency of the interauricular septum was found in Piper and Irvine-Jones's⁵ case. The usual finding is a systolic murmur over the apex. Burch⁹ found cardiac symptoms in 4 of his 8 cases. One of the patients succumbed to heart disease. Only 1 patient (case 5) of this series was affected, and he had only a slight mitral murmur at the apex.

OCULAR CHANGES

The ophthalmologic features are those associated with ectopia lentis, iridodonesis, contracted pupils which react only sluggishly to atropine and irregularity of the anterior chamber of the eye. Bilateral dislocation of the lenses is the outstanding symptom. The lens may be dislocated in any direction, upper displacement being the common type. Although most authors speak of dislocation of the lens, it is actually subluxation in most cases. Complete dislocations have been reported by Thaden¹² and by Weve.⁴ Young³ in 1929 analyzed the 22 reported cases with 4 of his own. In 9 of these no mention was made of the ocular findings. Of the remaining cases, dislocation of the lenses was present in 30 per cent, iridodonesis in 38 per cent, miosis in 38 per cent, megalocornea in 8 per cent, a persistent pupillary membrane in 8 per cent, amblyopia in 8 per cent and a shallow anterior chamber in 8 per cent. The globes were deeply set in about 30 per cent. No abnormal changes were found in the fundi. Weve⁴ found ocular complications in 50 per cent of 84 reported cases, in 33 per cent of these cases there was ectopia lentis. The lenses frequently show partial or complete opacity.

¹¹ Borger F. Ueber zwei Falle von Arachnoidaktylie, *Ztschr f Kinderh* **12** 161, 1914.

¹² Thaden F. Ein Fall von Arachnoidaktylie mit besonderer Berücksichtigung der Augensymptome, *Arch f Augenh* **100** 278 1929.

TREATMENT

Some patients with myopia and astigmatism have been benefited by suitable lenses. Improvement in vision usually results from removal of the lens in cases in which it is completely dislocated. Spinal curvature in none of these patients (cases 1, 2 and 3) was severe enough to require treatment. Pain in the foot may necessitate the use of supports. Finger contractures may be treated, with improvement in function (case 3).

SUMMARY AND CONCLUSIONS

1 Six cases illustrating various features of the syndrome of anachmodactyly are reported.

2 Microscopic examination of muscle tissue in 2 cases showed no pathologic change.

3 Certain roentgen and contracture peculiarities of the hands and feet have been pointed out.

REACTIONS OF THE PERITONEUM TO TRAUMA AND INFECTION

FURTHER EXPERIMENTAL STUDIES

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In a consideration of the more common complications which occur after abdominal operations it is evident that none is more serious than peritonitis and none more deserving of careful study from the standpoint of both prevention and cure. While the incidence of postoperative peritonitis has gradually and steadily declined during the past several decades, the possibility of its occurrence remains one of the chief hazards of operations on the lower part of the intestinal tract, and this is particularly true when resections or anastomoses which involve the large bowel are performed. The general decrease in the occurrence of postoperative peritonitis has been the result of (1) improvements and standardization in operative technic, (2) perfection in anesthesia, and (3) a greater realization of the importance of a proper period of meticulous preoperative care. During this period (seven to ten days or more) the fluid and electrolyte balances are restored and nutritional disorders are corrected. Thus, states of hypoproteinemia or anemia are corrected by blood transfusions, vitamin deficiencies overcome by the appropriate therapy and depleted glycogen stores replenished by a liberal carbohydrate intake.

For many years abdominal surgeons have observed and commented on the fact that the dangers of postoperative peritonitis are considerably less when laparotomies are performed on patients who have had colostomies or rectal or intestinal fistulas for some time than when the operation is performed on a patient with an intact or virgin peritoneum. Moreover, in the selection of the safest operative procedure in dealing with such lesions of the colon as carcinoma, it has been suggested by some writers that operation in stages is indicated since they contend one of the chief advantages of the multiple stage procedure is the immunity conferred on the peritoneum by the first operation which usually involves some form of intestinal anastomosis.

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About a year ago a series of experiments was conducted by Brinkman and one of us¹ in an effort to determine in a quantitative fashion the extent of such protection afforded by some of the more common abdominal operations. Dogs were used in the experiments, and a study was made of the effects of simple exploratory laparotomy as well as intestinal anastomoses performed at different levels in the digestive tract.

The conclusion from these earlier studies was that there is an enhanced resistance to infection which results from surgical manipulations in the peritoneal cavity. In dogs this is insufficient to protect the animal against a severe form of peritonitis, although such protection is possible by other means, e. g., intraperitoneal vaccination. A striking example of such protection is seen following the administration of a preparation of colon bacilli, aleuronat and tragacanth (coli-bactragen) developed by Steinberg. It was also concluded that phagocytosis in the peritoneal cavity is an important factor in the survival of dogs with acute peritonitis and that the polymorphonuclear leukocyte is the important cell in the phagocytosis and consequent recovery. It should be repeated here that in dealing with experimental peritonitis there are certain differences between the reactions of the peritoneum of the dog and that of man. In the dog, adhesion formation is minimal, there being little attempt at walling off of infections by the peritoneum. Furthermore, there are technical difficulties attendant on the production of a uniformly fatal lesion by inoculation of the peritoneal cavity with many of the standard cultures. Frequently one produces typical fibrino-purulent peritonitis, which, however, does not result fatally, whereas on the other hand, as the result of excessively large doses of bacteria the animal may succumb and the peritoneal cavity at necropsy exhibit none of the morbid changes characteristic of peritonitis.

On the basis of Steinberg's² extensive experiences, in which he was successful in producing peritonitis by intraperitoneal inoculation with the colon bacillus suspended in tragacanth, we have adhered to this method of producing experimental peritonitis. In the present study we have used his culture *Bacillus coli* no. 300, employing twenty-four hour agar cultures.

This paper reports the results of our more recent experiments concerning quantitative determinations of the peritoneal immunity which results from various abdominal operations.

1 Collier, F. A., and Brinkman, H. Studies on the Reaction of the Peritoneum to Trauma and Infection, *Ann. Surg.* **109** 942 (June) 1939.

2 Steinberg, B. Experimental Background and Clinical Application of Coli and Gum Tragacanth Mixture (Coli Bactragen), *Am. J. Clin. Path.* **6** 277 (May) 1936.

The quantity of culture material used for the inoculation is designated in terms of slants of twenty-four hour agar cultures, the dose ranging in most instances from one fourth of a slant to two slants. According to careful calculations, the washings from one slant were estimated to contain approximately 5,000 000 000 organisms.

TABLE 1—*Determination of Minimum Lethal Dose*

Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Or gram in	Phagocytes	Poly morpho nuclears %	Mono nuclear %	W B C (Peritoneal Fluid)
663	Control	1/20 slant	Recovered	2 hr 4 hr 24 hr	— 0 0	0 0 0	97 97 97	1 2 3	15 000 19 000 30 000
664	Control	1/20 slant	Recovered	2 hr 4 hr 24 hr	No fluid obtained + 0	0 0 0	98.2 97.1	1.8 2.9	12 000 21 000
665	Control	1/10 slant	Recovered	2 hr 4 hr 24 hr	No fluid obtained + 0	0 0 0	97 95	3 2	9 000 22 000
667	Control	1/5 slant	Recovered	2 hr 4 hr 24 hr	0 + 0	0 0 +	98.6 98.3 97.1	1.4 1.7 2.0	6 500 8 100 33 000
664	Control	1/4 slant	32 hr	4 hr 24 hr 32 hr	— ++ ++	0 0 0	96 86 77	4 14 2	6 900 39 000 34 000
669	Control	1/4 slant	Recovered	4 hr 24 hr 48 hr	+ 0 0	0 0 0	91 82 95	9 18 5	23 000 150 000 224 000
669	Control	1/4 slant	Recovered	4 hr 24 hr 48 hr	— 0 0	0 0 0	94 93 97	6 2 3	Fluid in sufficient 112 000 73 000
669	Control	1/4 slant	Recovered	4 hr 24 hr 48 hr 96 hr	— 0 0 0	0 0 0 0	97 96 95 98	3 4 5 2	31 000 50 000 42 000 Fluid in sufficient
668	Control	1/2 slant	8 hr	4 hr 8 hr	++ +++	0 0	94 82	6 18	21 000 67 000
661	Control	1/2 slant	10 hr	1 hr 4 hr 10 hr	— + ++	— — 0	89 76 64	11 24 26	4 000 34 000 39 000
668	Control	1/2 slant	17 hr	2 hr 4 hr 17 hr	++ + +++	0 0 0	90 81 89	10 19 11	5 800 14 400 24 000
670	Control	1 slant	46 hr	4 hr 8 hr 24 hr 46 hr	++ ++ ++ +++	— 0 0 0	76 89 54 60	24 29 46 40	9 100 9 500 63 000 51 000

METHOD AND RESULTS

Determination of the Minimum Lethal Dose of B. Coli—The first problem was to determine the minimum lethal dose of *B. coli* for the normal dog. In the first experiment the following doses of the colon bacillus were given intraperitoneally: 1/20, 1/10, 1/5, 1/4, 1/2, 1, and 2 slants. After the inoculation, peritoneal fluid was removed at various intervals by means of a fine capillary pipet. The total cell count of the fluid was determined as was the percentage of polymorphonuclear leukocytes and large mononuclear cells. The relative number of free organisms in the fluid was estimated at these different times. The findings are shown in table 1. It was found that a dose of one-half slant was almost

invariably fatal, while a smaller dose was not. Doses larger than one half slant were always fatal.

One half of one slant having been established as the minimum lethal dose for the normal dog, various abdominal operations, presently to be described, were performed.

Effect of Abdominal Operations on the Peritoneum—In order to determine whether a surgical operation gives protection against subsequently induced peritonitis, two criteria were used. The first was the survival or death of the animal, a rather crude but nevertheless convincing method. It was not sufficiently precise, however, to indicate finer gradations of protection. The second, more delicate index was determination of the cellular response as well as of the relative number of free organisms in the peritoneal exudate.

Because of the prevailing belief that a colostomy affords considerable protection against peritonitis from subsequent operations, the effect of a colostomy on the

TABLE 2—*Inoculation Two Weeks After End Colostomy*

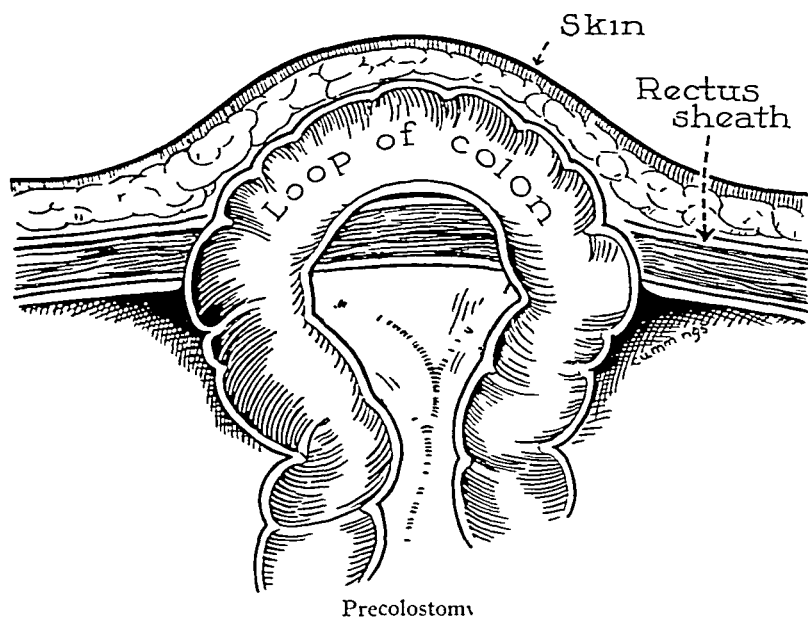
Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Organisms	Phagocytosis	Poly morpho nuclears, %	Mono nuclears, %	W B C (Peritoneal Fluid)
722	End colostomy	1/4 slant	18 hr	Post mortem	++	0	88	12	295,000
719	End colostomy	1/4 slant	Recovered	24 hr	0	0	97	3	310,000
720	End colostomy	1/2 slant	11 hr	Post mortem	+	0	90	10	241,000
700	End colostomy	1/2 slant	7 hr	Post mortem	+++	+	84	16	140,000
704	End colostomy	1 slant	10 hr	Post mortem	++	+	85	15	220,000
716	End colostomy	1 slant	6 hr	Post mortem	+	0	90	10	231,000
666	Control	1/4 slant	Recovered	24 hr	+	0	98	2	103,000
688	Control	1/2 slant	17 hr	Post mortem	++++	0	89	11	24,000

peritoneum was first studied. Six healthy dogs were selected and end colostomies performed in the routine manner, the distal portion of the colon being used. The animals were allowed to convalesce for two weeks, at the end of which time peritonitis was induced, doses of 1/4, 1/2 and 1 slant respectively being given to each of 2 dogs. Two normal dogs were used as controls. The results of these experiments are given in table 2. It will be noted that only 1 of the colostomized dogs, 1 that received only one fourth of a slant (less than the minimal lethal dose) recovered. As compared with the controls, the important findings in the peritoneal fluid of these animals were (1) a markedly increased number of leukocytes within a few hours after the inoculation and (2) a definitely smaller number of free organisms. The polymorphonuclear leukocyte was found to be the predominant cell in the exudate. From these experiments we concluded that the peritoneum showed no evidence of greatly increased resistance to infection two weeks after the establishment of a colostomy. However, judging from the increase in leukocytes in the peritoneal cavity and the small number of free organisms, it is felt that there was some tendency toward protection.

In order to determine whether the degree of protection was dependent on the interval between operation and the production of peritonitis, colostomies

TABLE 3—Inoculation One Month After End Colostomy

Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Organisms	Phagocytosis	Polymorpho nuclei %	Mono nuclei %	W B C (Peritoneal Fluid)
737	End colostomy	1/4 slant	Recovered	2 hr	—	—	90	10	3500
723	End colostomy	1/2 slant	6 hr	Post mortem	++	0	88	12	96000
721	End colostomy	1 slant	8 hr	Post mortem	+++	0	90	7	128000
718	End colostomy	2 slants	5 1/2 hr	Post mortem	+++	0	91	9	132000
738	Control	1/4 slant	Recovered	2 hr	—	+	96	4	4100
740	Control	1/2 slant	9 hr	Post mortem	+++	0	62	36	212000



were again performed and peritonitis similarly produced at the end of four weeks. With this longer interval no greater protection was obtained (table 3).

In order to determine the reaction of the peritoneum to purely mechanical irritation in instances in which there is no factor of fecal contamination, further experiments were undertaken by means of the operation illustrated. A laparotomy was performed and a segment of the distal part of the colon approximately 8 cm long was drawn through the incision and implanted subcutaneously. For convenience this operation is referred to as a precolostomy. Such an operation was performed on each of 8 dogs. Again at the expiration of two weeks, peritonitis was induced by intraperitoneal inoculation with varying doses of colon bacillus (table 4).

It will be noted from a study of this table that there was evidence of considerable protection in this group. Both dogs receiving the minimum lethal dose recovered. Also 1 that received two times and another that received four times the minimum lethal dose survived. It is of interest that in 1 instance (dog 678) in

which the implanted loop slipped back into the peritoneal cavity five days after operation the animal died, whereas dog 680, which received an equal dose, recovered. Once more it was observed that in this entire group of animals as compared with the controls the peritoneal fluid contained a large number of leukocytes but few extracellular organisms.

Furthermore, in the dogs which recovered there was a higher percentage of polymorphonuclear leukocytes than in the control dogs, emphasizing the importance of this cell in phagocytosis.

TABLE 4—*Inoculation Two Weeks After Precolostomy*

Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Or ganisms	Phago cyto sis	Poly morpho nuclears, %	Mono nuclears, %	W B C (Peritoneal fluid)
668	Control	½ slant	8 hr	4 hr	++	0	94	6	21,000
				8 hr	+++	0	82	18	60,000
673	Control	1 slant	46 hr	4 hr	++	+	76	24	9,100
				8 hr	++	0	80	20	9,500
				24 hr	++	0	54	46	63,000
				46 hr	++++	0	60	40	51,000
674	Precolostomy	¼ slant	Recovered	4 hr	+	+	99	1	368,000
				24 hr	0	0	97	3	536,000
				48 hr	0	0	93	7	330,000
				96 hr	No fluid obtained				
677	Precolostomy	¼ slant	Recovered	4 hr	0	++	96	4	332,000
				24 hr	0	0	94.8	5.2	314,000
				48 hr	0	0	95	5	281,000
				96 hr	No fluid obtained				
681	Precolostomy	½ slant	Recovered	4 hr	+	0	97	3	393,000
				24 hr	0	+	94.8	5.2	420,000
				48 hr	0	0	92.3	7.7	431,000
				96 hr	0	0	93.2	6.8	418,000
682	Precolostomy	½ slant	Recovered	4 hr	+	+	98	2	102,000
				24 hr	0	+	95.1	4.9	52,000
				48 hr	0	0	94.6	5.4	480,000
				96 hr	0	0	92.7	7.3	367,000
675	Precolostomy	1 slant	24 hr	4 hr	++	0	94.3	5.7	320,000
				24 hr	++++	0	81	19	60,000
679	Precolostomy	1 slant	Recovered	4 hr	0	++	97.5	2.5	52,000
				24 hr	0	0	97.6	2.4	461,000
				48 hr	0	0	93.7	6.3	111,000
				96 hr	0	0	92.5	7.5	596,000
680	Precolostomy	2 slants	Recovered	4 hr	0	+	93.5	6.5	201,000
				24 hr	0	++	96.0	4.0	229,000
				48 hr	0	+	97.6	2.4	214,000
				96 hr	0	0	95.4	4.6	210,000
678	Precolostomy	2 slants	23 hr	4 hr	+	0	90	10	514,000
				23 hr	++++	0	81	19	11,000

Having found this evidence of a fairly marked protection as the result of precolostomy, we selected an additional group of 10 dogs. Precolostomies were performed in a similar fashion. However, in this group of animals, instead of inducing peritonitis two weeks after the operation, we simply opened the subcutaneous colostomy at this time, producing an artificial anus in the abdominal wall. Two weeks after the opening of the loop peritonitis was induced. The results are shown in table 5. Contrary to our expectations, there was considerably less evidence of protection in these animals than in those in which the peritoneum had been left intact. In fact, there was actually less evidence of protection than in normal dogs. The 2 dogs that received ¼ slant died, whereas the normal dogs will tolerate a dose of this size. The peritoneal exudate contained a marked increase in the number of leukocytes. In an attempt to rationalize this

TABLE 5—*Inoculation Two Weeks After Opening Colostomy*
(*One Month Postoperative*)

Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Or gam-mes	Phago cyto-sis	Poly morpho-nuclears %	Mono-nuclears %	W B C (Peri-toneal Fluid)
696	Opened pre-colostomy	1/4 slant	18 hr	Post mortem	—	+	89	11	180 000
697	Opened pre-colostomy	1/4 slant	20 hr	Post mortem	++	0	84	16	150 000
701	Opened pre-colostomy	1/2 slant	22 hr	Post mortem	++	0	75	25	212 000
695	Opened pre-colostomy	1 slant	7 1/2 hr	Post mortem	+	+	79	21	114 000
699	Opened pre-colostomy	1 slant	6 hr	Post mortem	+	—	84	16	59 000
705	Opened pre-colostomy	1 slant	18 hr	Post mortem	—	0	90	10	58 000
710	Opened pre-colostomy	1 slant	21 hr	Post mortem	++	0	87	13	32 000
709	Opened pre-colostomy	2 slants	5 hr	Post mortem	++	—	80	20	48 000
670	Opened pre-colostomy	1/2 slant	8 hr	Post mortem	++—	—	88	12	29 000
671	Opened pre-colostomy	1/2 slant	6 hr	Post mortem	++++	+	95	5	42 000
679	Control	1/4 slant	Recovered	8 hr	+	0	91	9	16 000
691	Control	1/2 slant	10 hr	Post mortem	—++—	—	83	17	5 000

TABLE 6—*Inoculation Four Days After Removal of Peritoneum*

Dog No	Procedure	Dose	Survival Time	Time of Smear	Relative Number Free Or gam-mes	Phago cyto-sis	Poly morpho-nuclears %	Mono-nuclears %	W B C (Peri-toneal Fluid)
729	Removal of peritoneum	2 slants	Recovered	4 hr 24 hr	++ 0	++ 0	92 92	8 8	312 000 490 000
730	Removal of peritoneum	2 slants	Recovered	4 hr 24 hr	0 0	++ 0	95 97	5 3	514 000 620 000
731	Removal of peritoneum	2 slants	Recovered	4 hr 24 hr	0 0	++ +	98 98	2 2	600 000 54 000
732	Removal of peritoneum	2 slants	Recovered	4 hr 24 hr	0 0	++ 0	89 95	11 5	426 000 590 000
734	Removal of peritoneum	2 slants	Recovered	4 hr 24 hr	— 0	++ 0	92 96	8 4	420 000 598 000
735	Removal of peritoneum	2 slants	20 hr	4 hr 20 hr	— —	++ 0	94 87	6 13	386 000 328 000
736	Removal of peritoneum	2 slants	18 hr	4 hr 18 hr	— ++	— ++	90 84	10 16	490 000 478 000
737	Control	2 slants	Recovered	4 hr 24 hr	— 0	— 0	91 97	9 3	484 000 612 000
738	Control	2 slants	Recovered	4 hr 24 hr 48 hr	— 0 0	— 0 0	95 95 97	5 2 3	530 000 540 000 514 000

Coli bacteria two days after operation

it might be suggested that the increase in the interval between the operation and the production of peritonitis was significant. Thus it seems probable that the protection derived from the laparotomy is largely lost after such a long interval. We found this to be true also in earlier experiments reported in a previous communication. It was not our impression that the decreased protection was due to malnutrition or to any debility resulting from the colostomy.

Effect of Partial Removal of Peritoneum on Vaccination—In view of the fact that it is often necessary in certain abdominal operations to remove large areas of peritoneum, experiments were planned to investigate the effect of such a procedure on vaccination. The operation consisted in removal of a large portion of the parietal peritoneum from both sides of the abdominal wall. The incision extended the entire length of the abdomen, and the parietal peritoneum was removed as far posteriorly as the vertebral column. Slight hemorrhage was encountered, and the wounds healed by primary union. Two days after removal of the peritoneum as described an attempt was made to produce hyperleukocytosis by the injection of coli-bactrugen into the abdominal cavity. It has been shown repeatedly by Steinberg that this method of producing peritoneal leukocytosis is practically infallible in the normal dog. It has also been demonstrated by him that such a leukocytic response affords marked protection against subsequently induced peritonitis. Two days after the administration of the coli-bactrugen or four days after operation peritonitis was induced, living cultures of the colon bacillus in large doses being used. The results are shown in table 6, and it will be noted that the 2 controls recovered, as did 5 of the 7 dogs. In all of the animals, both controls and those with a portion of the peritoneum removed, there was a consistently high leukocyte count in the peritoneal fluid. There was a marked predominance of polymorphonuclear leukocytes in the dogs which recovered, this predominance being less marked in the animals which died. It was our conclusion that even in the absence of a fairly large portion of the peritoneum a greater protection was afforded by this method of peritoneal vaccination than was obtained by any of the operations described.

COMMENT

If these experimental studies may be applied to the human patient, it would seem on the basis of peritoneal "immunity" alone that there is little argument in favor of operation in stages. Other factors, however, which may be of greater importance than that of immunity, must be seriously considered, and the experimental studies presented here are not to be interpreted as a condemnation of multiple stage operations. Undoubtedly the formation of adhesions, with the walling off of definite compartments within the peritoneal cavity, is an important function of the peritoneum which helps to prevent general peritonitis at subsequent operations. Of significance also is the fact that in multiple stage operations the function of a colostomy or intestinal anastomosis becomes well established prior to the resection, whereas otherwise the physiologic adjustment of the intestinal tract to this alteration is superimposed on a major surgical procedure.

When complicating factors, such as obstruction, perforation or abscess formation are present, the necessity for stage operations is quite evident.

Finally the lessened trauma from a smaller operation may be desirable for the debilitated patient

We appreciate the fact that these studies have not given the final answer to many of the controversial questions which arise in dealing with peritonitis, but we hope that they will serve to stimulate further investigation along these lines

CONCLUSIONS

Under the conditions of the foregoing experiments it seems that abdominal operations confer on the peritoneum some degree of resistance to infection. This resistance is not marked however and is less than that which can be obtained by intraperitoneal vaccination. The protection derived from operation was of short duration, being uniformly less at the end of one month than at the end of two weeks after operation. The greatest degree of protection was observed after subcutaneous implantation of an unopened loop of colon (precolostomy) in which there was no factor of infection other than that incidental to an exploratory laparotomy. Removal of a large portion of peritoneum had little if any effect on the mobilization of leukocytes in the abdominal cavity after intraperitoneal vaccination (coli-bactragen). Careful microscopic examination of the peritoneal fluid at varying intervals after the production of peritonitis revealed that the polymorphonuclear leukocyte was the important cell as far as phagocytosis was concerned.

STAGES IN PERITONITIS BASED ON THE DEFENSE MECHANISM IN RELATION TO TREATMENT

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Peritonitis is an inflammatory process similar in its fundamental character to inflammation elsewhere in the body but modified by the functional activities peculiar to the peritoneum. Absorption of diffusible bacterial toxins, passage of bacteria, omental migration and intestinal motor activity are some of the pertinent processes which determine the outcome of peritoneal inflammation. The nature of the invading bacteria and the host's protective response supply most of the variable factors which modify the course of the disease. Since inflammation is essentially a defense measure, the local lesion of the peritoneum is necessarily a protective mechanism. The systemic effects may be considered results of the struggle between the infecting bacteria and the host.

In order to evaluate the relative significance of the factors in peritonitis, it is essential to determine the histologic progression of the disease, the progressive exudative changes and the nature of the damage to the host. It is obvious that within the space allotted neither experimental investigations nor clinical correlations can be detailed, hence, only a summary of conclusions is presented.

NATURE OF THE DEFENSE MECHANISM

Polymorphonuclears constitute the most important factor in the local struggle¹. Probably there are additional elements, such as fibrin, opsonins, and other antibodies, which may or may not play some part in the defense. The role of these elements is considered negligible except in certain conditions of bacterial invasion, such as pneumococcal infection. Shortly after the onset of peritonitis, the circulating polymorphonuclears show an appreciable drop in numbers. This drop com-

From the Department for Medical Research, Toledo Hospital

Read before the Section on Surgery, General and Abdominal, at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939

1 (a) Steinberg, B., and Snyder, D. A. Immune Cellular Reactions in Experimental Acute Peritonitis, *Arch Path* 8:419 (Sept.) 1929. (b) Snyder, P. F. A. Inflammatory Reaction in the Omentum, *Arch Path Inst d Univ Helsinki* 7:453, 1933

cides with the appearance of leukocytes in the peritoneal exudate² The next phase in the leukocytic picture is the surrender of the leukocytes by the tissue reservoirs³ Owing either to some stimulating factor or factors or to withdrawal of leukocytes from the circulation and tissue depots, the tempo of bone marrow activity is accelerated and more leukocytes are poured into the circulation These cells eventually find their way into the peritoneal cavity The peritoneal exudate reveals rapid

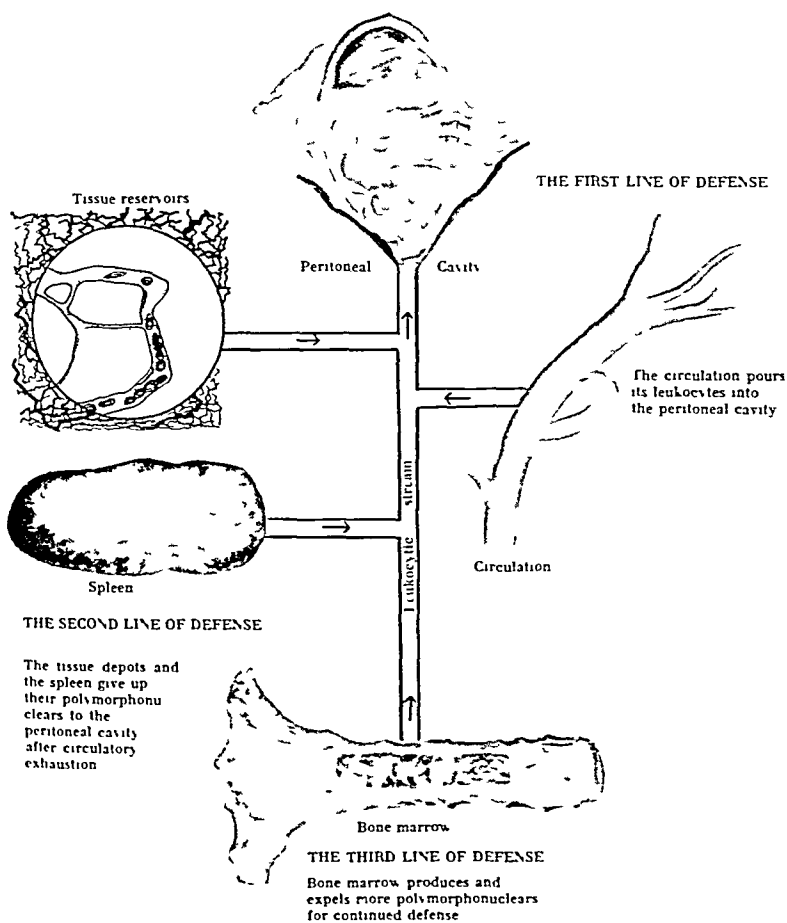


Fig 1—Defense mechanism against peritonitis It is shown to consist of mobilization and migration of polymorphonuclears into the peritoneal cavity

2 Pons, C A , Gannon, J M, and Belk, W P Withdrawal of leukocytes in Experimental Peritonitis, *Am J Clin Path* 5 225 (May) 1935 Steinberg and Snyder 11

3 Golubandt, P Experimental Investigations on Spleen Changes in Peritonitis, *Virchows Arch 1 path Anat* 272 783 1929

phagocytosis by the polymorphonuclears of the invading bacteria. This ingestion is complete within a very short period. Survival is invariably associated with complete removal of bacteria. Death, on the other hand, is consistent with a gradually increasing number of free peritoneal bacteria and with polymorphonuclear insufficiency.⁴ An experiment may be cited to demonstrate the role of the polymorphonuclears. When leukocytes produced in one animal are injected into the peritoneal cavity of another animal with otherwise lethal peritonitis, the subject survives and shows complete phagocytosis of the bacteria.⁵ The defense may be summarized as consisting of rapid and sufficient mobilization of polymorphonuclears in the peritoneal cavity.

INHIBITORY MECHANISM

Absorption from the peritoneal cavity is probably one of the more pertinent of the processes which determine the outcome of the infection. Absorption is accomplished through the medium of the lymphatic vessels and the serosal capillary bed.⁶ There is considerable evidence that bacteria choose the lymphatics for a principal pathway and that soluble toxic substances are carried off largely by the capillaries. It must be emphasized, however, that both the capillaries and the lymphatics are capable of removing either the larger, particulate bacteria or the smaller, crystalloid bacterial toxic substances.⁷ Inflammation of the peritoneum alters the mechanism of removal of contaminants from the peritoneal cavity.⁸ When the inflammatory process persists for a certain period, removal of bacteria is markedly diminished, and the relatively few micro-organisms that escape do so through the lymphatic channels.⁹ On the other hand, soluble, diffusible substances, such as bacterial toxins, continue to be absorbed.¹⁰ These soluble toxic substances reach the

4 Steinberg, B. A Rapid Method of Protecting the Peritoneum Against Peritonitis, *Arch Surg* **24** 308 (Feb) 1932

5 Steinberg, B. Transfer of Living Leukocytes and the Effect on Acute Infectious States, *Arch Path* **25** 785 (June) 1938

6 Bolton, C. Absorption from Peritoneal Cavity, *J Path & Bact* **24** 429 (Oct) 1921. Wells, H. G., and Johnstone, O. P. On the Route of Absorption of Bacteria from the Peritoneal Cavity, *J Infect Dis* **4** 582 (Nov) 1907. Steinberg, B., and Goldblatt, H. Studies on Peritonitis. II. Passage of Bacteria from the Peritoneal Cavity into Lymph and Blood, *Arch Int Med* **39** 449 (March) 1927

7 Buxton, B. H., and Torrey, J. C. Studies in Absorption, *J M Research* **15** 3, 1906

8 Miller, R. G. The Influence of Inflammation on the Absorption of Substances of Varied Diffusibility, *J Exper Med* **67** 619 (April) 1938

9 David, V. C. Peritonitis. Experimental Study, *Surg, Gynec. & Obst* **45** 287 (Sept) 1927

10 Steinberg, B. The Cause of Death in Acute Diffuse Peritonitis, *Arch Surg* **23** 145 (July) 1931

various viscera and induce damage. The myocardium, because of the nature of the heart, is perhaps the most important structure so affected.¹¹ An experiment demonstrates the mechanism just described. Introduction of a homologous antiserum or an antitoxin into an experimental animal with diffuse peritonitis results in survival providing administra-

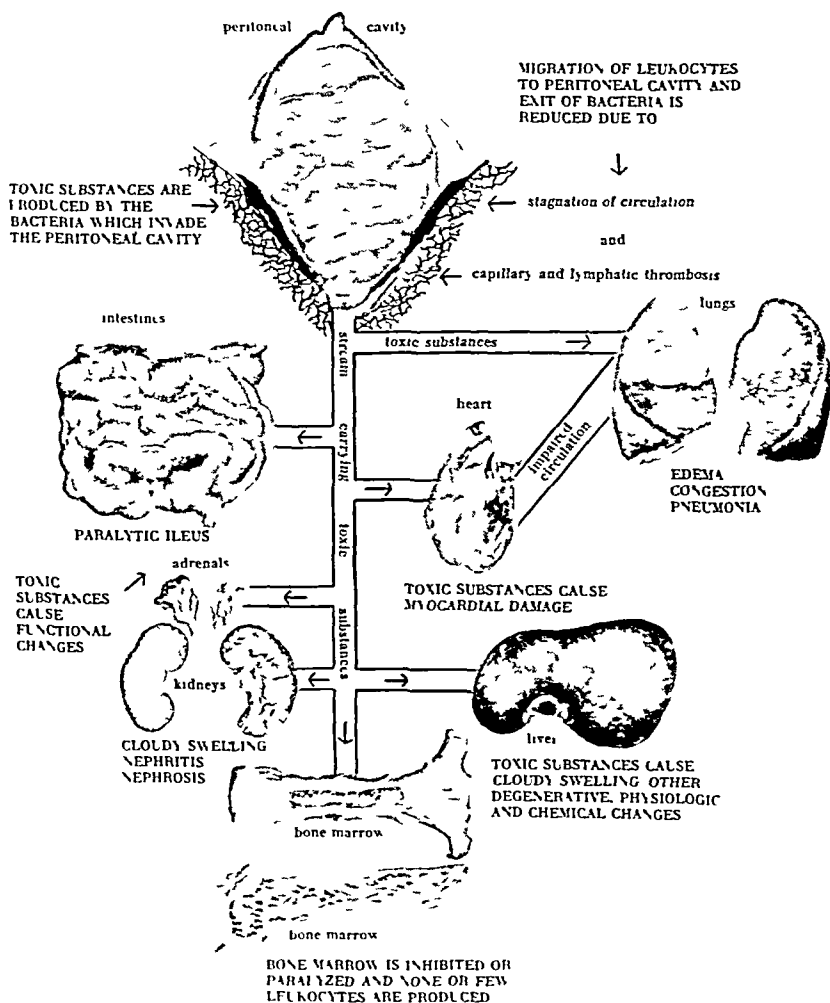


Fig 2—Inhibitory mechanism in the defense against peritonitis

¹¹ Steinberg B, Kobacker J L, and Russell, T G Cardiovascular System in Acute Experimental Peritonitis *Proc Soc. Exper Biol & Med* 30 1155 (May) 1933 Steinberg B, and Kobacker, J L The Cardiovascular System in Protected and Unprotected Animals with Acute Diffuse Peritonitis, *J Lab & Clin Med* 20 1180 (Aug) 1935

tion is done prior to irreversible myocardial damage¹⁰ Evidences of the effects on the heart of the toxic substances are deduced from studies of electrocardiographic tracings and determinations of continuous blood pressure during the course of peritonitis^{11b}

The histologic progressive changes of the peritoneal tissue result from the effect of the invading bacteria and the reaction on the part of the host After onset of peritonitis, there is a period of bacterial inactivity corresponding to the "bacterial lag," an adaptation of the microorganisms to the new environment The inflammatory process during this period is slight Bacteria pass from the peritoneal cavity into the circulation, and leukocytes enter the cavity After the bacteria adapt themselves to the peritoneum, they begin to multiply and induce an inflammation of a greater degree There are consequent slowing and (later) stagnation of the circulation, with capillary and lymphatic thrombosis As a result, the rate of bacterial passage is markedly diminished, and by the same token polymorphonuclears enter the peritoneal cavity in considerably smaller numbers After a certain interval the bacteria begin to produce soluble toxic substances which diffuse through the peritoneum to reach the various viscera When the time of action of the toxic substance is sufficiently prolonged, the visceral damage becomes irreversible and permanent, and death ensues

STAGES IN PERITONITIS

On the basis of the local peritoneal struggle, the systemic responses to the infection and the protective and inhibitory mechanisms, peritonitis may be divided into three stages Each stage can be interpreted in terms of both the local peritoneal change and the systemic effects

The first (primary) stage lasts for approximately eighteen to twenty-four hours and corresponds to the period of bacterial inactivity and maximum efficacy on the part of the host's defenses Bacteria are removed from the peritoneal cavity, and their destruction is accomplished by a threefold process local peritoneal phagocytosis, bactericidal activity of the blood and the activity of the reticuloendothelial system Since the peritoneal tissues are only slightly affected by the inflammatory process at this stage, polymorphonuclears enter the peritoneal cavity in large numbers and are available for phagocytosis of the bacteria At this stage, enhancement of the host's defenses is indicated whenever they are found insufficient to cope with the infection The primary stage may terminate with recovery when bacterial destruction is accomplished, or it may continue into the next (secondary) stage

The secondary stage of peritonitis lasts from twelve hours to three days, depending on the virulence and the number of the invading bac

teria and the degree of resistance¹² of the patient. The stage is initiated by a marked bacterial proliferation and sufficient inflammatory tissue changes of the peritoneum to interfere with bacterial passage and leukocytic migration. The defense mechanism of the body is at a low point, but artificial enhancement in the early period may aid in overcoming the infectious process. The local struggle is the only measure of defense in this stage. Destruction of bacteria terminates this stage, and failure of destruction of bacteria results in progression of the disease to the final (tertiary) stage.

The tertiary stage is characterized by the elaboration of bacterial toxic substances with their diffusion from the peritoneal cavity and their effect on the viscera. The stage lasts from twelve hours to three days, depending on the titer of the toxic substances and their quantitative neutralization by antibodies which may be harbored by the patient. The pertinent effects of the toxic substances are on the bone marrow and the myocardium. The activity of the one is inhibited or paralyzed, and serious circulatory impairment results from the action on the other. The host's defense mechanism is incapacitated. Treatment obviously should be directed toward neutralization of toxic substances and preservation of the integrity of the vascular system. The damage accomplished in the late tertiary stage is irreversible and irreparable.

DETERMINATION OF THE STAGES

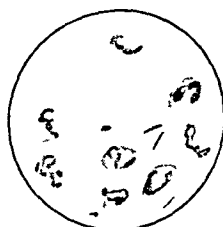
Although clinical manifestations may furnish sufficient evidence for the establishment of the stages in peritonitis, a quantitative procedure is obviously more satisfactory. Correlation of experimental methods in various problems in peritonitis with clinical material established a relatively simple criterion for differentiation of the stages. Since repeated investigations indicated that the local peritoneal picture reflects the defensive and the inhibitory mechanisms of the host, the peritoneal exudate was utilized for determination of the stages. It was found that the number of free bacteria in the exudate constitutes a simple and reliable guide¹³. On this basis the stages are differentiated according to the number of free bacteria in an average field. The primary stage is characterized by the presence of six or less free bacteria. The phagocytosed micro-organisms are disregarded. The secondary stage is

12 Resistance is interpreted to include the activity of the bone marrow, leukocytic migration, a competent circulatory system and a ready response on the part of the reticuloendothelial system.

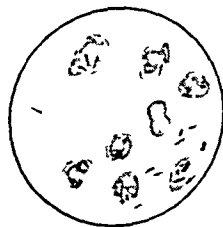
13 Steinberg B. Peritonitis to be published.

denoted by the presence of six to ten free bacteria, and the tertiary stage, by more than ten free micro-organisms

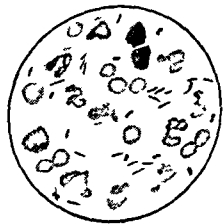
The exudate may be obtained either at operation or by abdominal puncture. The time consumed by the technical details should not exceed



PRIMARY STAGE



SECONDARY STAGE



TERTIARY STAGE

Fig 3—Determination of the stages of peritonitis

a few minutes. Smears are stained with Wright's and Gram's stains, the free bacteria are counted in ten fields and an average in one field is calculated. Such a rapid determination of the stage offers a visual picture of the relative state of the defensive and inhibitory mechanisms of the patient and allows the choice of treatment.

TREATMENT IN RELATION TO THE STAGES

Since the primary and the early part of the secondary stage of acute diffuse peritonitis allow the normal defenses of the host to be mobilized against bacterial invasion, the defense may be enhanced by artificial means. During this period, mobilization of polymorphonuclears in the peritoneal cavity is unrestricted by the physical changes apparent later in inflammation. Since these leukocytes constitute the essential element in the defense any procedure which stimulates their production and accomplishes their local mobilization should be utilized. Experimental

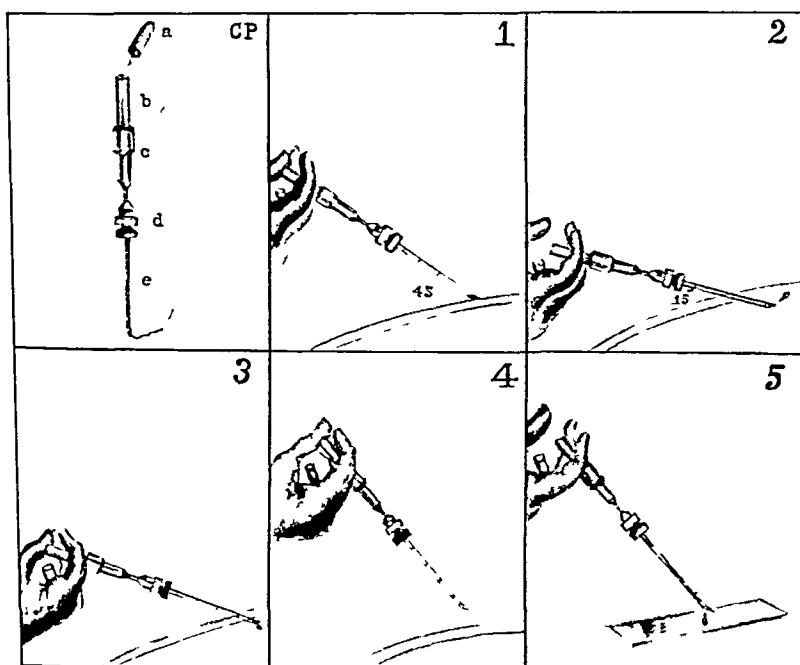


Fig 4—Method of testing CP capillary pipet for obtaining small volumes of peritoneal exudate by abdominal puncture. Note (a) rubber cap, (b) capillary glass pipet, (c) steel or silver capillary, (d) movable guard and (e) 2 inches (5 cm) of a graduated capillary needle. 1 introduction of the needle through the abdominal wall with the thumb covering the lumen of the glass capillary so as to prevent blood from entering the needle during its passage through the abdominal wall. 2 removal of the thumb while the needle is laid down to form an angle of 15 degrees between the shirt and the abdominal wall. 3 attraction of peritoneal exudate to the capillary bore (capillary attraction). 4 exudate filling the glass capillary. The thumb is placed over the capillary and the needle is drawn out, expelling a drop of the exudate on a glass slide.

investigations and clinical applications have demonstrated that introduction into the peritoneal cavity of a satisfactory "leukocyte stimulating and mobilizing substance" suspended in tragacanth accomplished those

purposes.¹⁴ Later in the secondary stage, with inhibition of the host's defensive measures, such stimulation is obviously of little or no value. Treatment should be directed to conserving the circulatory system, stimulating the bone marrow and aiding phagocytosis in the peritoneal cavity by the available leukocytes. These purposes may be accomplished indirectly by complete rest, administration of morphine and

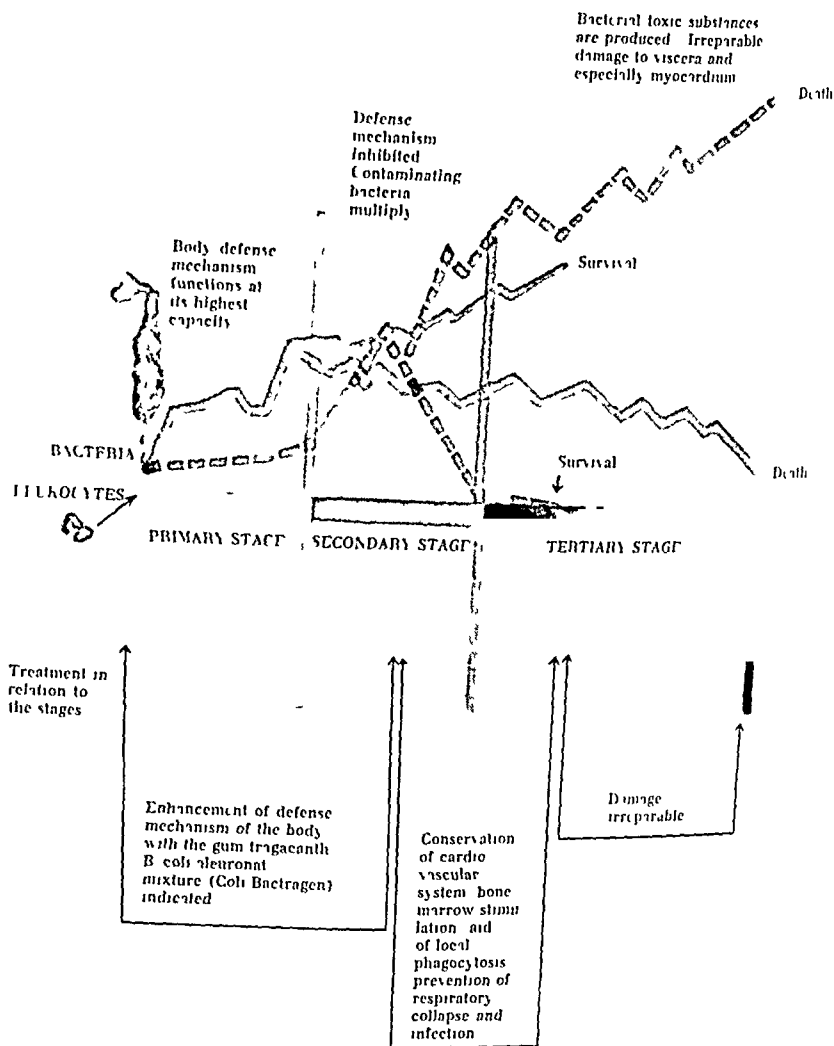


Fig 5—Schematic representation of the stages in peritonitis in relation to the defense mechanism and to treatment

avoidance of any additional intestinal motor excitants. Administration of oxygen, with frequent periods of inhalation of carbon dioxide (to pre-

¹⁴ Steinberg, B. An Improved Method of Protecting the Peritoneum of Dogs Against Fatal Colon Bacillus Infection, *Proc Soc Exper Biol & Med* 29 1018 (May) 1932. Steinberg, B., and Goldblatt, H. Protection of Peritoneum Against Infection, *Surg, Gynec & Obst* 57 15 (July) 1933. Steinberg, B. The Experimental Background and the Clinical Application of the Escherichia Coli and Gum Tragacanth Mixture (Coli-Bactragen) in Prevention of Peritonitis, *J Clin Path* 6 253 (May) 1936.

vent bronchial occlusion and pneumonic lesions), and daily small blood transfusions serve further to accomplish the desired effects. Since water and food cannot be taken by mouth, these substances should be administered by intravenous introduction of not over 3,000 cc of physiologic solution of sodium chloride and 500 cc of 10 per cent dextrose a day except in the presence of vomiting, when additional fluid should be given.¹⁵ Sodium chloride and dextrose should be administered cautiously.¹⁶ Excessive administration of sodium chloride and fluid will result in increase of peritoneal fluid¹⁷ and a greater effort for an already damaged heart. Treatment of the tertiary stage may follow that of the secondary but, although much can be done, little will be accomplished. The damage produced by the toxic substances in the late tertiary stage is irreparable.

SUMMARY

1 Peritonitis is divided into three stages. The division is based on the defensive and inhibitory mechanisms of the host.

2 The various factors operating in defense of the host against invasion by bacteria are enumerated. The inhibitory factors which militate against recovery are placed in their relation to the local and systemic changes.

3 A method of differentiation of stages is described.

4 Treatment of the various stages is associated with the defense and the inhibitory mechanisms.

ABSTRACT OF DISCUSSION ON PAPERS BY DRS COLLER, RANSOM AND RIFE AND DR STEINBERG

DR. F. A. COLLER (Ann Arbor Mich.) The peritoneum is an enormous serous surface that roughly approximates the surface area of the skin. It has an excellent blood and lymphatic supply and a generous supply of omentum, apparently designed for protection against bacterial and traumatic injury.

Infection of the peritoneum is occasionally primary but commonly secondary to infection originating in abdominal viscera. Formerly the peritoneum was opened with fear because it was thought that its resistance was low. More recently there has been ascribed to it a specific immunity that can be increased by the use of various vaccines. Dr. Steinberg has put forward a new conception of protection against infection through the production of local hyperleukocytosis artificially or through the reaction of the peritoneum to trauma and infection. His experimental work has shown that artificial production of hyperleukocytosis will protect against subsequently induced peritonitis.

¹⁵ Maddock, W. G., and Coller, F. A. Water Balance in Surgery. *J. A. M. A.* **108** 1 (Jan 2) 1937.

¹⁶ Coller, F. A., Dick, V. S., and Maddock, W. G. Maintenance of Normal Water Exchange with Intravenous Fluids. *J. A. M. A.* **107** 1522 (Nov 7) 1936.

¹⁷ Blalock, A. Effect of the Administration of Salt Solution on the Amount of Fluid That Accumulates in the Peritoneal Cavity. *Arch. Surg.* **26** 1098 (June) 1935.

Our work, like this, may be criticized as dealing with peritonitis produced by a single organism when we know that in clinical peritonitis there are many types of bacteria at work. However, we have used a certain strain of *B. coli* so that we could have a dose of bacteria that was lethal with a constant dosage. Dr. Steinberg has demonstrated that phagocytosis is the important local reaction and that any procedure such as the introduction of antiseptics or wiping the bowel to remove exudate interferes with this reaction and diminishes local resistance. This emphasizes the importance of minimizing manipulations in an abdomen which is the site of peritonitis.

One must emphasize the importance also of aid in maintaining all other physiologic activities of the body while the combat between the bacteria and the leukocytes is going on in the peritoneum.

The gastrointestinal tract must be kept at rest by prohibition of food, drink and cathartics. Distention, which decreases the vital capacity, must be combated by morphine and constant aspiration of the stomach and of the upper part of the small intestine. Dehydration, ketosis and hypochloration secondary to vomiting, aspiration and starvation must be corrected by proper administration of fluids. Anoxia due to distention, pulmonary complications or perhaps toxemia must be treated by oxygen therapy. Operative procedures must be limited to those that simply stop the infection at its source. One cannot overemphasize the importance of maintaining body function with these measures.

We have shown that trauma to the peritoneum produced by operation gives a small degree of protection against infection, but the immunity is not adequate to protect against severe degrees of infection.

In my experimental and clinical observations I find that the preliminary production of hyperleukocytosis does give protection against infection incurred at operation. However, in most operations, unless there is frank soiling of the peritoneum by operative mishap this protection is not necessary. If there is gross contamination, I now use a preparation of colon bacilli, aleuronat and tragacanth (coli-bactragen) at operation. In most operations I feel it is not necessary, nothing prevents postoperative peritonitis like careful, aseptic operative technique, and nothing aids the body in combating peritonitis after it is established like the maintenance of normal chemical and physiologic activity by use of the measures mentioned.

DR C F DIXON (Rochester, Minn.) The work of Dr. Collier and his associates closely coincides with that of Hermann, carried out about eight years ago.

I realize that there are some who believe that the use of vaccine as a preoperative safeguard against peritonitis is of no value. Some have even gone so far as to state that the intraperitoneal injection of vaccine is a dangerous procedure. Many thousands of such injections have been carried out for patients in the intestinal service at the Mayo Clinic without the occurrence of untoward results. For some years I have been of the opinion that the incidence of peritonitis following surgical operations on the colon has been definitely decreased by this maneuver. The vaccine we of the clinic use is essentially the same as that advocated by Dr. Steinberg, except that, in addition to colon bacilli, streptococci are included in the preparation.

During the past year I have used vaccine in the treatment of alternate patients in my service for whom operations were performed on the colon and ileum. The study is not yet complete, but an accurate statistical evaluation by one of my associates, Dr. W. J. Tennison, has reached the stage at which some deductions can be drawn, and it depicts the fact that deaths from peritonitis were fewer than

patients to whom vaccine was administered. In considering patients on whom abdominoperineal anterior resection or so-called exteriorization operations were performed, the mortality in the hospital among the group of patients receiving vaccine was only 6 per cent as compared to 17 per cent for patients who were not vaccinated.

For patients in whom gross soiling occurs, I have in many instances used a preparation of colon bacilli, aleuronat and tragacanth (coli-bactragen), recommended by Dr Steinberg.

Frequently the statement is heard "If good technique is employed, peritonitis will rarely occur." It is of course assumed that the surgeon invariably attempts to do his best, however, peritonitis still occurs, and I think it develops much more often if vaccine is not employed.

It seems to me that a sufficient amount of investigation has already been done on this subject to warrant the use of vaccine as a possible preventive procedure against peritonitis.

DR J. SHELTON HORSLEY (Richmond, Va.) Dr Steinberg has done a splendid piece of work in developing his coli-bactragen and in investigation of the pathogenesis of peritonitis.

The coli-bactragen as now prepared, with formaldehyde-killed, instead of heat-killed *Escherichia coli*, is better than the earlier product because it attains maximum efficiency in a few hours and can be used at the time of operation. I use it consistently in operations on the colon or in any other operations in which peritonitis may be anticipated. It is, of course, not a panacea and cannot cure a leaking suture, but I am confident of its value and would not do without it.

The coli-bactragen itself is a preventive of peritonitis. It is not a treatment for well established peritonitis, but Dr Steinberg's suggestion of producing leukocytes in one animal and injecting them into another may lead to a cure in developed peritonitis.

My two sons and I reported on 972 operations for appendicitis between Jan. 1, 1931, and May 1, 1939. There were 85 cases of perforated appendix with abscess and localized peritonitis and 34 cases of spreading or diffuse peritonitis. In the latter group only 1 patient died. There were six deaths in the whole series of 972 cases.

Since Jan. 1, 1931, we have adopted five points in the treatment of appendicitis. We have added the use of suction in every case of abscess or peritonitis. We never sponge or place gauze in the peritoneal cavity in such cases. Complete rest is given to the bowel by avoidance of proctoclisis and by administration of dextrose in Ringer's solution intravenously. Of course this is necessary only in case of abscess or peritonitis. The three points which we had been and are still stressing are (1) immediate operation at any stage of appendicitis, (2) the McBurney incision and (3) simple ligation of the stump of the appendix.

DR W. WAYNE BIRKBECK (Philadelphia) With interest aroused by Dr Steinberg's work I have used coli-bactragen in a few cases and have seen unexpected recovery after heavy peritoneal contamination.

Unfortunately in many cases one is as yet unable to increase the resistance of the body sufficiently to overcome the peritoneal infection. Three other factors in peritonitis should constantly be borne in mind. The first is the initial bacterial contamination which of course is a chief concern of aseptic surgical practice. The second is the propagating factor—the blood, the necrotic tissue, the serum, the bile, the intestinal contents or the culture medium in which an otherwise harmless number of bacteria may multiply into an overwhelming horde and then swarm.

through the cavity in numbers beyond the capacity of the phagocytes and other protective elements to destroy. Spreading peritonitis is a liquid-borne disease. The third factor is the serous or other fluid that carries the bacteria from one part of the peritoneal cavity to another. I have attempted, with encouraging results, to prevent the diffusion of bacteria within the peritoneal cavity by internal exteriorization. Large, open glass tubes (lamp chimney drains) are anchored over a localized abscess, necrotic tissue, a septic gallbladder, a gangrenous appendix or a questionable line of intestinal suture, so that evacuation may occur with the peritoneum protected by isolating adhesions.

I have also removed liquid culture medium and diffusing fluid from the abdominal cavity after operations in which bacterial contamination was feared by the use of aspirating or Sump drains. These are double tubes of glass, the outer tube perforated and the inner tube connected with a continuously acting aspirator pump. By these drains a relatively dry peritoneum may be maintained for several days. Differing from rubber and other drains now used, glass drains may remain in the human peritoneal cavity for several days without plastic exudate or adhesion. Therefore, drainage of the peritoneal cavity, heretofore often considered impossible, is feasible at least for two or three days provided that only glass drains are used. By constant attention to these four factors, diffuse peritonitis in many cases may be prevented or arrested.

DR BERNHARD STEINBERG (Toledo, Ohio) I should like to reemphasize Dr. Collier's warning that the patient as a whole must be treated and not only a part of him, such as the peritoneal cavity. Limitation of time prevents stressing this important element in the original presentation.

I should like to emphasize also that the problem of peritonitis, which has been considered for many years only from the mechanical point of view, is also one of physiologic, chemical, bacteriologic and immunologic concern. It is therefore essential to recognize the nature and the scope of the role played by these factors in peritonitis.

PERITONITIS IN CATS PRODUCED BY INTRA-PERITONEAL INJECTION OF BACILLUS COLI SUSPENDED IN MUCIN

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NEW YORK

Numerous attempts have been made to produce bacterial peritonitis in animals. In some experiments attempts were made to enhance the pathogenic effect of bacteria by preliminary treatment of the peritoneum of laboratory animals with a great variety of substances: turpentine (David¹), agar (David and Loring²), croton oil (Pawlowsky³), potato (Halsted⁴), omental ligation (Halsted⁴), sarcolin (Solieri⁵), intestinal juices (Blalock⁶) and tragacanth (Benians,⁷ Steinberg⁸).

*Ralph Colp Fellow in Bacteriology

From the Laboratories of the Mount Sinai Hospital

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(Footnote continued on next page)

In other experiments different inoculums were tried feces (Herrmann⁹), fecal emulsions (Wilen and Dragstedt¹⁰) and contents of small intestines (Pawlowsky³). The intestinal tract has been employed as the source of peritoneal infection by ligation of the appendix (Costain,¹¹ Lehman¹²), division of the appendix (Blalock¹³), ligation of the mesoappendix (Blalock¹³), perforation or incision of the gastrointestinal tract at different levels (Bergh¹⁴) or drainage of an open loop of ileum into the peritoneal cavity (Buchbinder¹⁵). Mucin has been found of definite value in increasing the virulence of induced bacterial infections in mice and rats (Nungester, Jourdonais and Wolf¹⁶). The micro-organisms employed in combination with mucin were as follows: *Streptococcus haemolyticus*, *Staphylococcus aureus*, *Bacillus coli*, *Staphylococcus albus*, *Bacillus subtilis*, *Micrococcus*

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catarrhalis, nonmucoid Friedlander bacillus, anthrax bacillus meningococcus (Rake,¹⁷ Proom,^{17a} Cohen^{17b}), gonococcus (Miller and Castles¹⁸), *Bacillus typhosus* (Henderson, Jameson and Powell¹⁹) and pneumococcus (Nungester and Jourdonais,¹⁶ Gunn and Nungester²⁰)

In view of the considerable irregularity of results obtained by most of these methods, the work described was undertaken in order to develop a standardized method for producing experimental peritonitis

MATERIAL, METHOD AND RESULTS

The strains of micro-organisms employed were as follows

B. coli (Lewis, S-6, "A" and "R" [from human bowel], "RF" [from rabbit stool], "F" "AL" and "O" [obtained during a diarrhea epidemic], P M 677 [taken post mortem from a subject with peritonitis] and many others obtained from subjects with renal sepsis, acute appendicitis and cholangitis), *Enterococcus* "E" (rabbit stool), and *B. typhosus* "TL"

The mucin used was the granular variety (Wilson Laboratory). It was prepared for intraperitoneal injection according to the method of Rake^{17c} except that an electric egg beater was employed for a few minutes to break up the mucin suspension instead of the mucin being allowed to soak as in Rake's method. Tragacanth solution was made up according to the procedure of Steinberg⁵

The strains of *B. coli* used were grown for eighteen to twenty-four hours on plain agar slants at 37 C. These slants were washed off with saline solution, and the organisms were suspended and diluted in physiologic solution of sodium chloride. Dilution was adjusted so that 1 cc. contained 900,000,000 organisms according to a standard barium sulfate nephelometer.²¹ The bacterial suspensions

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TABLE 1—Results of Inoculation with B Coh Alone and in Combination with Mucin, Tragacanth and "Animal Transfer"

Animal	Group No	Strains	Dose	Enhancement	Animal Passage	Total No	Died		Survived	
							Peri tonitis	No Peri tonitis	Peri tonitis	No Peri tonitis
Rabbit	1	Lewis	90,000 to 900,000,000	Mucin in some	0	13	0	4	0	9
Rabbit	2	SG, "F", "A", "D", "AD", P M 677	9,000,000 to 900,000,000	Mucin	0	20	0	3	0	17
Rabbit	3	P M 677	9 000,000 to 1,800,000,000	Mucin, tragacanth	+	26	4	5	1	16
Rabbit	4	P M 677 (smooth colonies) renal sepsis acute appendicitis, cholangitis	1,800,000,000	Mucin tragacanth	+	8	1	2	1	4
Rabbit	5	Rabbit feces (control)	2 to 10 cc saline suspension	Mucin and none	0	7	6	1	0	0
Rabbit	6	Enterococcus "L" colon bacillus "RI"	900,000 000 to 1,800,000,000	Mucin	0	12	2	1	0	9
						86	13	16	2	55

were then diluted, and "pour" plates of low dilutions were made for bacterial counts. With this method the error due to dilution was comparatively small (i e., ± 10 per cent). Organisms suspended in saline solution alone and in saline solution and mucin were injected into the peritoneal cavities of animals with a large bore needle (16 or 18 gage) and syringes of 20 and 50 cc capacity. Autopsy was performed on all dead animals as soon as possible, usually within one to six hours after death, and cultures were made of the peritoneal fluid and heart's blood in dextrose broth. The surviving animals were killed in a few days to one week after the injection. Intravenous injection of ether or air proved the simplest method of killing the animals. Blood for culture was obtained from rabbits and cats during life by intracardiac puncture. Various tissues were removed for histologic examination. Peritoneal fluid for cytologic and bacteriologic studies was withdrawn by means of peritoneal punctures with an 18 gage needle with a syringe attached. In this manner intestinal trauma was avoided. The experimental animals were of both sexes and miscellaneous breeds except as otherwise indicated. They were in a good state of nutrition and were quarantined prior to the experimental work.

As may be seen from the results recorded in table 1, a total of 86 rabbits was employed in attempts to produce experimental peritonitis. A variety of strains of *B. coli* and enterococcus, alone and in combination with mucin and tragacanth, were injected into the peritoneal cavity. The virulence of some strains was enhanced by passage through animals prior to the experiments. Moreover, some animals received rabbit feces intraperitoneally. After the treatment described, 29 rabbits died, and 57 survived for from three to seven days before they were killed. Seven of the rabbits that died (and most of those which received rabbit feces) showed evidence of peritonitis. There was a small amount (10 to 30 cc) of serosanguineous fluid in the peritoneal cavities of these animals. The intestines were not dilated, and there was no evidence of any purulent exudate. In some instances the vessels of the mesentery were engorged. No lymphadenopathy was observed. One animal had a volvulus of the intestine, which may have contributed to the peritonitis. Still another had pneumonia involving several lobes in addition to the peritonitis. Three of these 7 animals showed scattered areas or only a single area of localized fibrinous peritonitis. The attempts failed to elicit regularly an easily reproducible purulent peritonitis under standard conditions in rabbits.

However, the strains of *B. coli* which had passed through mice (4 times) and rabbits (10 times) when injected with mucin into rats produced peritonitis.

It is noteworthy (table 1 group 6) that the minimal lethal peritonitis-producing dose was 5,000 times less with mucin than with saline solution (90,000 and 450,000,000 organisms respectively).

In view of the encouraging results with rats, a series of experiments applying the aforementioned method was carried out in cats, as follows:

Ether given by inhalation or pentobarbital sodium given intravenously was employed at the onset in preparation for cardiac and peritoneal punctures and aspirations. Later, however, these procedures were performed in unanesthetized cats. After some preliminary work with various strains of *B. coli* (table 3, groups 1 and 2) a good peritonitis-producing strain was isolated. Moreover, the virulence of the strain was increased by passage through cats (table 3, groups 3-8). Mucin and tragacanth were both employed as enhancing agents. With the former, doses of *B. coli* as low as 45,000,000 were capable of causing a fatal peritonitis, whereas with the latter 270,000,000 organisms were required. Sixty-three

TABLE 2—*Inoculation of Mice and Rats with B. Coli and B. Typhosus Enhanced by Mucin*

Animal	Group	Strain	Dose	Enhancement	Animal Passage	Total No	Died		Survived	
							Peri tonitis	No Peri tonitis	Peri tonitis	No Peri tonitis
Swiss mouse	1	'I', 'AD', 'D'	90 to 90 000	Mucin	0	10	0	1	0	9
Swiss mouse	2	Typhoid TI	Loopful	Mucin in 1	0	2	1	0	0	1
Swiss mouse	3	P M 677	9,000	Mucin in 1	0	2	1	0	0	1
Swiss mouse	4	P M 677	9 to 9,000	Mucin (except one)	+	5	3	0	1	1
Swiss mouse	5	P M 677	9 to 900	Mucin in some	+	9	3	1	1	4
Rat	6	P M 677	90 000 to 900,000 000	Mucin	+	24	16	3	1	4
						—	—	—	—	—
				Totals for mice		28	8	2	2	16

TABLE 3.—*Inoculation of Cats with Various Strains of B. Coli, in Saline, Mucin and Tragacanth*

Group	Strain	Dose	Innancement	Animal Passage	Total No	Results		Survived		Cultures		
						Died of Perit. tonitis	No Perit. tonitis	Perit. tonitis	No Perit. tonitis	Blood Culture	Heart	Perit. toncum
1	P M 677	1 500 000 000	Mucin	+	1	1		3			1 +	1 +
2	P M 677	3 000 000 000 to 1 500 000 000	Mucin (1) and tragacanth	+	8	1	2	5			3 +	3 +
	I M											
3	R	1 000 000 000 to 1 500 000 000	Mucin	+	8	0	1	1			0 +	0 +
4	R	1 000 000 000 to 1 500 000 000	Tragacanth or saline	+	9	2	1	6			3 +	2 +
											1 negative	3 negative
5	R	9 000 000 to 1 500 000 000	Mucin	+	15	11		4		10 +	12 +	31 +
										1 negative	1 negative	1 negative
6	R	900 000 000 to 5 000 000 000	Tragacanth	+	13	11	1	1		5 +	1 +	0 +
										1 negative	1 negative	2 negative
7	R	7 200 000 000 to 9 000 000 000	Saline	+	3	2	1	1		1 +		2 +
										1 negative		1 negative
8	R	9 000 000 to 63 000 000	Mucin	+	19	15		4		1 + in those died	1 in dead	1 in dead

million organisms in 10 cc of mucin regularly produced fatal purulent peritonitis (table 4, group 3) Thus, the minimum lethal peritonitis-producing dose was 42 times greater with gum tragacanth than with mucin and regularly produced with the latter (table 4, groups 1-3)

Blood cultures were made in a great majority of cases, and these were found to yield *B coli* as early as one and one-half hours after intraperitoneal injection of the *B coli*-mucin mixture In the cases of the animals which succumbed the blood cultures usually yielded bacteria four and eight hours after the injections The greater the dose of organisms injected intraperitoneally, the more overwhelming was the bacteremia With very large doses (4,500,000,000) innumerable organisms were recovered in the blood, whereas with doses from 90,000,000 to 1,800,000,000 the colony count was 10 to 100 per cubic centimeter of blood

Peritoneal aspiration (after injection of organisms) demonstrated a variety of white cells, mainly polymorphonuclear leukocytes but including mononuclears, lymphocytes and mesothelial cells Organisms were found free and also within phagocytic cells In cases in which the peritonitis terminated fatally the number of organisms was very large, whereas in the surviving animals it was minimal (5 to 10 per oil immersion field)

TABLE 4—*Summary of Experiments on Cats with Mucin and with Tragacanth as Enhancing Agent*

Group	Strain	Dose	Inoculum	Total No	Died Peritonitis	Percentage
1	(Rafal) human <i>B coli</i>	9,000,000 to 4,500,000,000	Mucin	100	85	85
2	(Rafal) human <i>B coli</i>	900,000,000 to 5,400,000,000	Gum tragacanth	20	14	70
3	(Rafal) human <i>B coli</i>	63,000,000	Mucin	41	41	100

Necropsy in cases of death from peritonitis showed diffuse purulent peritonitis with dark yellow and yellow-green thick pus varying in amounts from 30 to 100 cc The blood vessels of the parietal and visceral peritoneum were engorged Both large and small intestinal loops were distended and rigid The mesenteric nodes were often enlarged and succulent Fibrinous exudate with a dull red luster was frequently observed on the visceral and parietal layers of the peritoneum Histologic sections verified the gross appearance An acute inflammatory exudate (mainly polymorphonuclear leukocytes) was present throughout the serosa of the intestinal wall and usually reached down to the muscularis

COMMENT

In 1925, Steinberg,⁸ following the work of Bemans,⁷ described a method of producing experimental peritonitis in dogs with a broth suspension of an agar culture of *B coli* mixed with tragacanth 11 cc dose injected was 40 cc containing 8,000,000,000 bacterial cells Iruer and Moss²² elicited peritonitis in rabbits by means of gum tragacanth and *B coli* The peritonitis observed on postmortem examination

22 Trusler, H M, and Moss, J M The Treatment of Colon Peritonitis in Rabbits with *Escherichia Coli* Anti-Serum, Surg, Gynec & O 69 34-36 (Jan) 1939

of a serosanguineous type This was accompanied by septicemia The animals were successfully protected by an antitoxic anti-colon-bacillus serum (1 c, containing Shwartzman antibodies [Lilly])

It may be emphasized here that in the experiments of Trusler and Moss the rabbits never showed evidence of peritonitis similar to that seen in the human being The experiments reported in this paper demonstrated serosanguineous peritonitis in rabbits resembling the condition described by Trusler and Moss except that mucin instead of tragacanth was used as the enhancing agent

In contrast, however, when *B. coli* and mucin was given intraperitoneally to cats the minimal lethal dose necessary for the production of peritonitis was considerably smaller than in Steinberg's experiments Thus, a dose of 63,000,000 organisms produced fatal lesions, whereas Steinberg required as many as 8,000,000,000 per dog Moreover it is of interest that 63,000,000, the dose indicated, or a greater dose, produced the results recorded with absolute uniformity The pathologic process followed closely the human type, being consistently diffuse and purulent It differed, however, in that an invasion of the blood stream accompanied the local condition It is hoped that peritonitis elicited under standard conditions²³ may be of value in further studies on etiology and treatment Work in this direction is under progress and will be reported later

SUMMARY

The injection of a human strain of *B. coli* suspended in mucin invariably produced fatal suppurative bacterial peritonitis in cats The method employed was simple and lent itself to standardization The minimal dose for the production of lethal peritonitis was 63,000,000 organisms An identical method and technic were effective in the production of peritonitis in rats and mice but not in rabbits

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TUMOR OF THE THALAMUS

A VENTRICULOGRAPHIC ENTITY

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In surgery of the brain the policy has been evolved of pronouncing final judgment as to the operability and prognosis of a tumor only after exploration and microscopic examination. In few instances will the experienced surgeon feel prepared to predict with finality even the pathologic type of the tumor, not to mention its operability. Although a properly made ventriculogram will localize a tumor to a satisfactory degree, it usually cannot be relied on to show the type of tumor. In any instance in which the ventriculogram can be relied on to indicate an inoperable tumor, it provides valuable information to the surgeon.

Tumors arising in the thalamus are unique in this respect. The ventriculographic picture is unmistakable, and the tumor, because of its position if not because of its cell type, is clearly inoperable. Four cases are presented here to illustrate the cardinal ventriculographic features of tumor of the thalamus. Another case has been presented by McConnell and Childe¹.

In 3 of the cases reported here the diagnosis was proved by autopsy or by operation. In the fourth case there were clinical findings which together with the ventriculogram made the diagnosis sufficiently clear. The first case, that of J. P., was reported in a previous paper² but is incorporated here for additional emphasis.

REPORT OF CASES

CASE 1—J. P., a Negro aged 38, was referred to us by Dr. E. W. Anderson of Des Moines, Iowa, in January 1936.

Three months previously he had noticed severe pain in the back of the head and neck. After this he had vomited many times. He had become irrational and disoriented two weeks before admission to the hospital.

From the Departments of Surgery and Neurology, the neurosurgical service, College of Medicine, State University of Iowa.

1 McConnell, L. H., and Childe, A. E. Tumors Involving the Basal Ganglia, Lateral Ventricles, Brain Stem and Cerebellum, Arch. Neurol. & Psychiat. 37: 56-67 (Jan.) 1937.

2 Hyndman, O. R. Cerebral Pneumography. Ventriculographic Interpretation of Tumors In and About Third Ventricle, Aqueduct of Sylvius and Fourth Ventricle, Arch. Surg. 36: 245-291 (Feb.) 1938.

Examination—There were general tenderness to percussion of the skull, bilateral paresis of the sixth nerve, advanced bilateral papilledema and dehydration. The patient swayed when his heels were together and his eyes closed. There were continued choreoathetoid movements of the upper extremities, these were at first interpreted as cerebellar ataxia, but the patient performed the usual cerebellar tests well. There were complete astereognosis on the right side and loss of sensation to light touch. The patient frequently tried to wipe some phantom object from the right palm. There was overreaction to the light scratch of a pin.

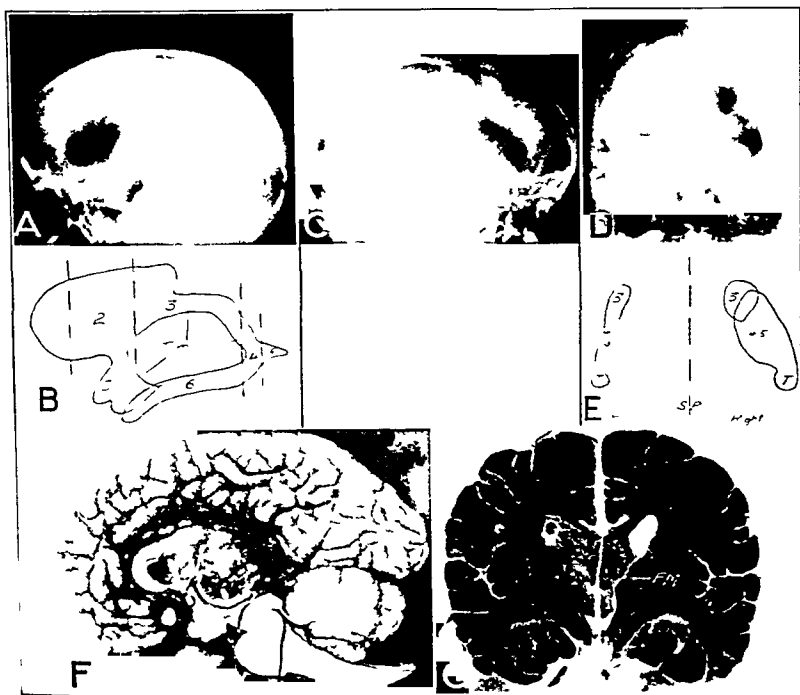


Fig 1—A, lateral view, right side down showing a filling defect in parts 3 and 4 and in the posterior two thirds of the third ventricle (Division of the lateral ventricle into parts 1 to 6 is in conformity with the scheme proposed by Torkildsen A and Penfield W. *Ventriculographic Interpretation Arch Neurol & Psychiat* 30 1011-1021 [Nov] 1933. The scheme is roughly indicated in B). B, diagrammatic representation of A. 3I indicates the third ventricle. C, lateral view, left side down showing the right ventricle. In a previous report² it was recorded that a filling defect existed in both lateral ventricles. Further study has corrected this interpretation. We feel that the point is important, because in none of these 4 cases was there a major filling defect in the contralateral ventricle. D, posteroanterior view (occiput up) illustrating the filling defect in parts 3 and 4. E, diagrammatic representation of D. T indicates the temporal horns (part 6). SP the mid-sagittal plane. F, photograph of the brain, illustrating how the tumor obliterates the posterior aspect of the third ventricle as well as the midline. The wire is through the aqueduct of Sylvius. G, photograph of the brain illustrating how in this case the tumor has actually invaded part 3 of the ipsilateral ventricle. H, W indicates the free margin of the tumor.

on the right arm, but this was not present on the left arm. The mental reaction was noteworthy. When spoken to or engaged in conversation the patient would often give rational answers, but as soon as he was left to himself he would mutter irrationally and call for his sister and mother.

There were advanced papilledema on both sides, generalized areflexia and a spinal fluid pressure of 590 mm of water with the patient in the prone position. Ventriculograms are shown in figure 1.

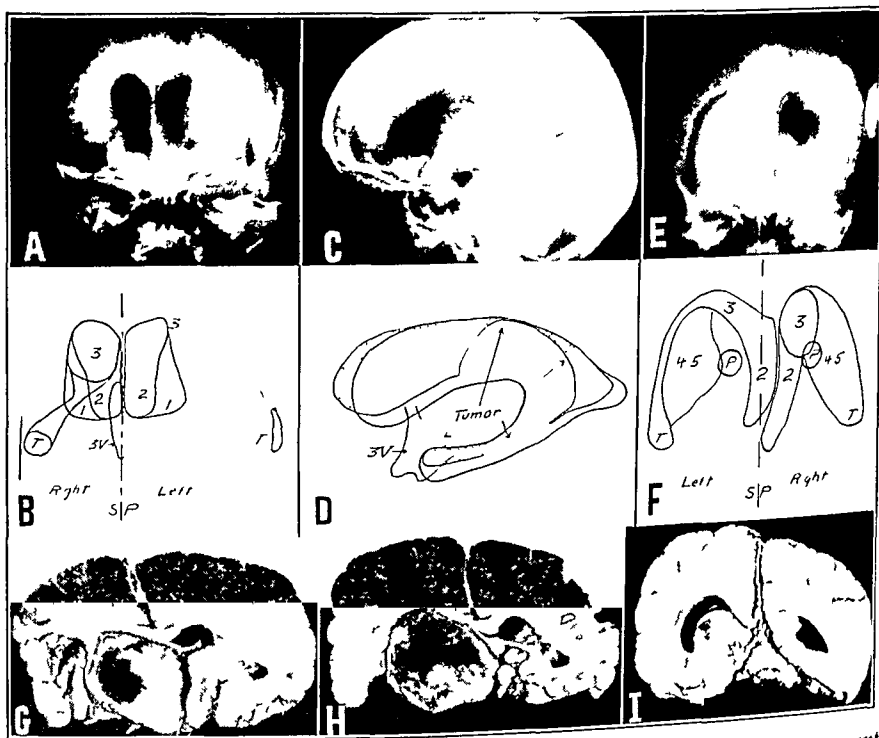


Fig 2—*A*, anteroposterior view (brow up), illustrating the following points: 1 After a complete filling of the ventricles with air the anteroposterior view is itself characteristic. 2 Air has found easy egress through the foramina of Monro to the opposite ventricle. (This was true in all cases.) 3 In spite of the size of the tumor the contralateral ventricle is normal in position and contour (except for uniform dilatation). 4 On the side on which the tumor is present there is a filling defect in the third ventricle; parts 1 and 2 show no filling defect, while parts 3 and 4 are markedly flattened upward and laterally and in this case part 6 is shifted laterally. *B*, diagrammatic representation of *A*. *T* indicates the temporal horns (part 6). *C*, lateral view, right side down, illustrating the sharply outlined filling defect in part 3 and most of part 4 of the left lateral ventricle and obliteration of the posterior aspect of the third ventricle. *D*, diagrammatic representation of *C*. The left lateral ventricle is stippled. *E*, posteroanterior view (occiput up), illustrating how part 3 and most of part 4 are flattened upward and laterally. It is stippled that part 5 (posterior horn) is shifted only a little from its normal position. *F*, diagrammatic representation of *E*. *P* indicates perforator openings, *T*, the temporal horns (part 6). *G*, *H*, and *I*, photographs of the brain, the sections being made anterior to part 4, through part 4 and behind part 4 respectively. They illustrate how the tumor encroaches on the third ventricle and flattens parts 3 and 4 of the ipsilateral lateral ventricle without encroaching on the contralateral ventricle. Figure 1 explains the presence of a shadow representing parts 4 and 5 in *F*. *P* indicates the pulvinar of the contralateral thalamus.

Operation—This was our first case of this kind, and exploration was done, material for biopsy being obtained through the corpus callosum. The tumor proved to be a glioblastoma. The patient died in the hospital, and postmortem examination revealed a tumor of the thalamus (fig 1 F and G)

CASE 2—H Z, a white woman aged 42, was referred to us by Dr D H Nord, of Cambridge, Iowa, on Aug 24, 1937

Her illness had begun in the spring, with loss of vigor numbness of the right side, awkwardness of the right leg and frontal headache

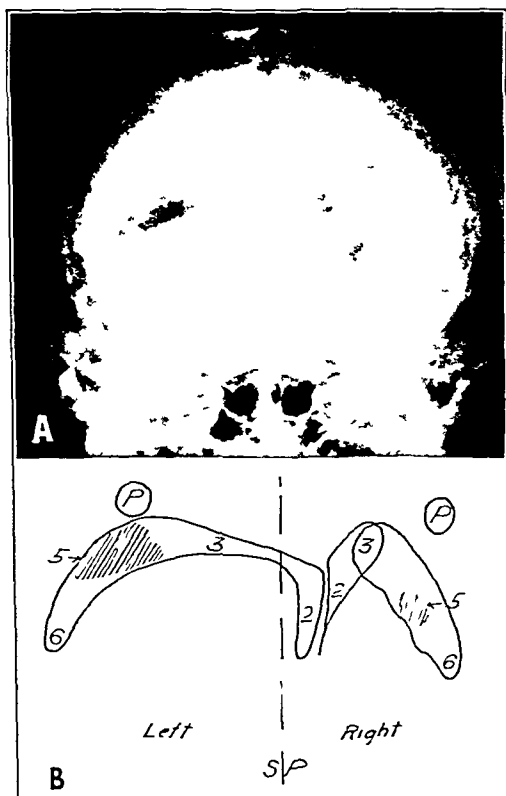


Fig 3—A posteroanterior view (occiput up) illustrating the upward and lateral flattening of part 3 on the left and in this case a lateral shift of parts 4, 5 and 6. B diagrammatic representation of A. P indicates periorbital opening, SP the mid sagittal plane

Examination—By August the patient was mentally confused and presented right hemiplegia, hemianesthesia and homianopia. The right pupil did not react to light. Although the optic disks appeared normal on admission, mild papilledema developed during hospitalization. The spinal fluid pressure with the patient in the prone position was 130 mm of water. Ventriculograms are shown in figure 2. A diagnosis of tumor of the thalamus was made. Operation was not thought justified.

The patient died in the hospital. The postmortem observations are shown in figure 2, *G*, *H* and *I*.

CASE 3—*R S*, a white man aged 47, was referred to us by Dr L A Miller, of North English, Iowa, on Nov 6, 1937.

Eight months previously his illness had begun, with "hot flashes" in the left arm and leg. These had been followed by "dizzy spells" lasting about five minutes. He had been nervous and drowsy and had complained of roaring in the left ear for two months.

Examination—There were a fine vertical nystagmus and right homonymous hemianopia. The spinal fluid pressure was 360 mm of water with the patient in the prone position. Examination otherwise gave essentially negative results.

A ventriculogram is shown in figure 3.

Operation—Through a small craniotomy opening an incision was made in the brain, the left posterior horn being exposed. It was then obvious that an expanding mass existed in the thalamus. A small biopsy specimen was obtained from the tumor, which proved to be a glioblastoma.

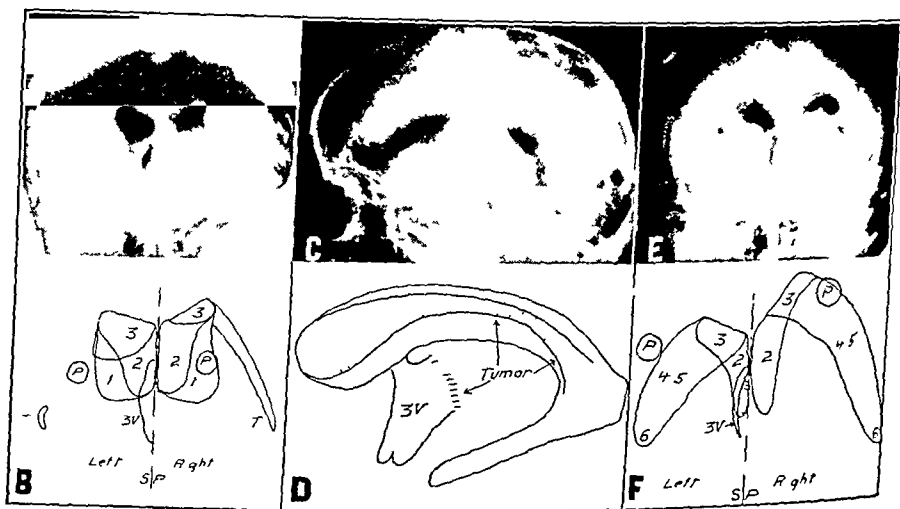


Fig 4—*A*, anteroposterior view, showing a filling defect in the right half of the third ventricle and part 3 flattened upward on the right. Except for dilatation the left lateral ventricle is normal in position and contour. *B*, diagrammatic representation of *A*. *P* indicates perforator openings. *C*, lateral view, left side down, showing obliteration of the posterior aspect of the third ventricle and flattening of part 3. *D*, diagrammatic representation of *C*. *E*, posteroanterior view showing a filling defect in the right half of the third ventricle and flattening of part 3. *F*, diagrammatic representation of *E*.

Course—The patient improved somewhat after a decompression and died three months later at home, after being restless and completely demented for two weeks.

CASE 4—*L K*, a white man aged 32, was referred to us by Dr John Warner of Davenport, Iowa, in June 1938.

His illness had begun four months previously, with weakness and numbness of the left foot. This progressed to involve the entire left side, so that at the time of admission the left side was hemiplegic and numb. He did not complain of headache.

Examination—There were total left hemiplegia and total left hemianesthesia. There was left homonymous hemianopia. There was no papilledema, and the spinal fluid pressure with the patient in the prone position was 85 mm of water. The mental status seemed unimpaired.

Ventriculograms are shown in figure 4, and a diagnosis of inoperable tumor of the right thalamus was made.

The patient died at home two months later, after a two day period of coma. Permission for postmortem examination was refused.

SUMMARY

Four cases of tumor of the thalamus are presented, with ventriculograms. The tumor was on the left side in 3 cases and on the right in 1. The tumors in the 3 cases in which the diagnosis was proved were glioblastomas. The time from the onset of symptoms until the diagnosis was made was three, five, eight and four months respectively. In each case the tumor was well advanced at the time the patient was seen in the hospital. The 4 patients died four, six, eleven and six months respectively after the onset of symptoms. The death of the first patient (J. P.) was no doubt hastened by the operation.

While one would certainly suspect a tumor of the thalamus from the clinical findings in all but case 3, the ventriculograms leave no doubt concerning the diagnosis.

It is of interest that in 2 cases the spinal fluid pressure was within normal limits and that in 3 cases, including these 2, papilledema was not present or developed late.

The ventriculographic pictures were all consistent and unmistakable, the two cardinal features being (1) flattening of part 3 upward and to the ipsilateral side, which can be seen in the anteroposterior view but more definitely in the posteroanterior view, and (2) obliteration of the posterior aspect of the third ventricle and the "negative" shadow of the massa intermedia.

Other features are the absence of filling defect in the contralateral ventricle, and the fact that little if any shift occurs in its position and the fact that parts 1 and 2 on the involved side remain intact and the foramina of Monro unobstructed. In some cases, depending on the size of the tumor, parts 4, 5 and 6 will be shifted to the ipsilateral side.

CONCLUSION

The ventriculographic findings in the case of tumor of the thalamus are consistent and unmistakable and indicate an inoperable tumor. (The cardinal signs are given in the summary.)

SCOLIOSIS FOLLOWING EMPYEMA

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A survey was made of the records of all the patients with non tuberculous empyema treated by operation in this institution during the years 1932 to 1936 inclusive. This study was undertaken because of the impression that scoliosis was an occasional sequel to operation for empyema. It was felt that careful observation of all the factors involved might explain why in some patients empyema was followed by persistent scoliosis while others, with apparently similar involvement, recovered without any permanent spinal deformity.

The observation has been made by Chandler¹ that in almost all cases of acute empyema scoliosis develops with the concavity toward the diseased side. This type of scoliosis is slight (18 degrees maximum) and in almost all cases subsides when the empyema is healed. Bisgard, Cleveland,³ Gaugele,⁴ Gurd,⁵ Hedblom,⁶ Kleinberg,⁷ Rey,⁸ Steindler⁹ and von Beust¹⁰ studied the problem of scoliosis in various types of

From the Surgical and Orthopedic Services of the Mount Sinai Hospital

1 Chandler, E. A., in discussion on Cleveland, M. Lateral Curvature of the Spine Following Thoracoplasty in Children, *J Thoracic Surg* 6 595, 1937

2 Bisgard, J. D. Thoracogenic Scoliosis. Influence of Thoracic Disease and Thoracic Operations on the Spine, *Arch Surg* 29 417 (Sept.) 1934, Skeletal Deformities in Children Resulting from Empyema and Methods of Prevention *J Thoracic Surg* 6 609, 1937, Acute Empyema. The Use of a Bradford Frame to Promote Dependent Drainage and to Prevent Scoliosis, *ibid* 6 624, 1937, Experimental Thoracogenic Scoliosis, *ibid* 4 435, 1935

3 Cleveland, M. Lateral Curvature of Spine Following Thoracoplasty in Children, *J Thoracic Surg* 6 595, 1937

4 Gaugele, K. Die postpleuritische Skoliose und ihre Verhütung, *München med Wchnschr* 66 442, 1919

5 Gurd, F. B. Scoliosis Accompanying Chronic Infected Open Pneumothorax, *Arch Surg* 5 366 (Sept.) 1922

6 Hedblom, C. A. Deformity of the Thorax Secondary to Pleural or Pulmonary Disease, *J A M A* 94 162 (Jan 18) 1930

7 Kleinberg, S. Scoliosis, New York, Paul B Hoeber, Inc., 1936

8 Rey, J. Die Bedeutung der postpleuritischen Skoliose im Kindesalter, *München med Wchnschr* 70 176, 1923

9 Steindler, A. Diseases and Deformities of the Spine and Thorax, St. Louis, C V Mosby Company, 1929

10 von Beust, A. T. Ueber den Einfluss der Rippenresection auf die Form der Wirbelsäule (Beitrag zu der Arbeit Hoeckels "Gibt es eine operative Behandlung der Skoliose?"), *Deutsche Ztschr f Chir* 158 154 1920

pulmonary disease. There are two main types of scoliosis resulting from intrathoracic disease.

1 Scoliosis following empyema. The concavity is toward the empyema and there is little or no rotation of the vertebral bodies.

2 Scoliosis complicating thoracoplasty. The convexity is toward the resected ribs.

There are exceptions to the rule, however, and the early curve may be convex on the side of the empyema if there is an extremely massive effusion. The curve resulting from thoracoplasty almost always has its convexity on the surgically treated side but may be influenced by the preexisting opposite curve caused by the empyema. Occasionally the two curves neutralize each other, and scoliosis following empyema with the concavity on the diseased side disappears after thoracoplasty.

This report is based on a study of all the patients with nontuberculous empyema treated by operation in the surgical services of the Mount Sinai Hospital from 1932 to 1936 inclusive who returned for examination of the spine. There was an opportunity to examine the spinal columns of 65 patients at the end of periods varying from one to six years after operation for empyema. These unselected patients represent one third of all those operated on and presumably comprise a representative sample.

Of the 65 patients, 5 had clinical evidence of scoliosis, but the curve was severe in only 2. By a severe curve is meant a deforming, obvious curve that cannot be hidden by clothing. Curves of 20 degrees or less may be considered slight and curves of 35 degrees or more, severe. In the 2 patients with severe curvature the primary curves were, respectively, 97 degrees and 44 degrees.¹¹

The case histories of the 2 patients with severe curvature follow. The curvatures were of contrasting types: the first had its convexity on the side of an extensive rib resection ("thoracoplasty scoliosis"), the second was concave on the side of the empyema, a typical post-empyemic curve.

REPORT OF CASES

CASE 1.—M. R., a boy aged 11 years at the time of admission (1930) entered the hospital because of cough and dyspnea of three weeks' duration. Physical and roentgen examination revealed a pleural effusion on the right side, pushing the heart and mediastinum to the left. It was noted on the roentgenogram that there was no spinal curvature at the time (fig. 1A). A stab thoracotomy and underwater drainage through the eighth intercostal space posteriorly were performed on the day of admission. A week later 1 inch (2.5 cm.) of the eighth rib was excised posteriorly and a large empyema cavity was drained of pus.

¹¹ Ferguson, A. B. Study and Treatment of Scoliosis. *South M. J.* 23: 116, 1930.



Fig 1 (case 1) —*A*, roentgenogram taken on admission of the patient to the hospital, three weeks after the onset of illness. At this time there was no evidence of a spinal curvature. *B*, roentgenogram taken nine months after onset of the illness. At that time a slight spinal curvature (5 degrees) was noted concave to the side of the empyema.

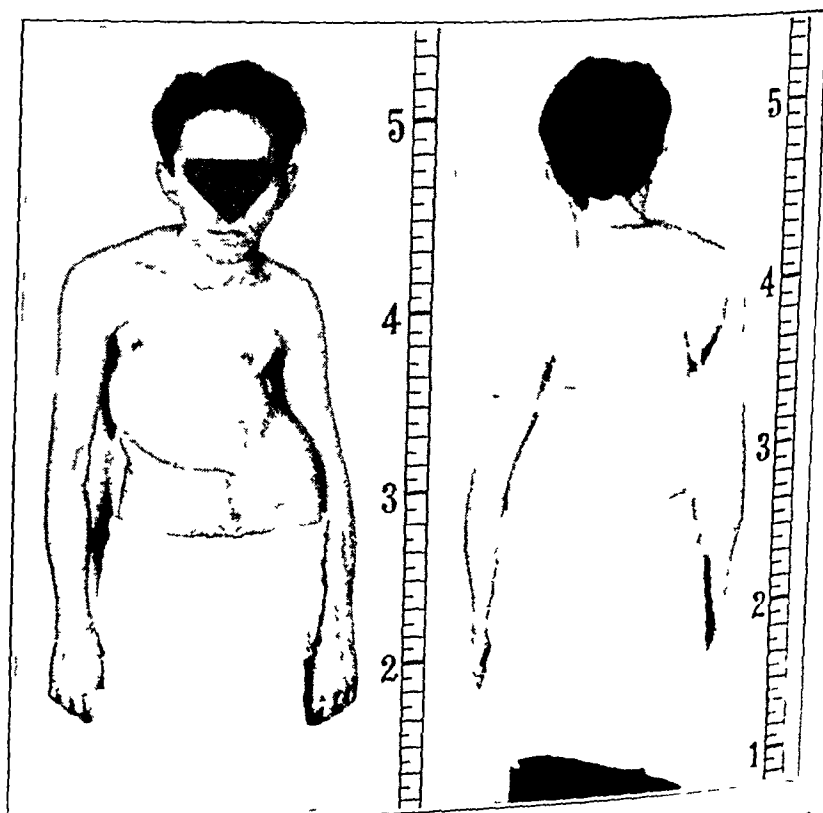


Fig 2 (case 1) —Appearance of the patient eight years after onset of illness.

containing *Pneumococcus* type I. One month later a portion of the ninth rib was excised posteriorly, and the lung was found markedly collapsed. The boy was readmitted eight months after the original operation, with chronic empyema. Roentgen examination on readmission revealed a slight (5 degree) curve, concave on the side of the empyema (fig 1B). A partial thoracoplasty consisting of resection of four ribs with intercostal tissues and pleura was performed in an attempt to obliterate a large intrapleural space. Nine months after the thoracoplasty, marked thoracic scoliosis, convex to the right, was noted. There was a compensatory lumbar curve to the left, the right shoulder was elevated and the right scapula prominent. Roentgen examination at this time revealed that the fifth to the tenth ribs inclusive had been resected. Soon after this, an unsuccessful attempt to correct the scoliosis by means of Risser (hinged) jackets was made in another institution. Three and three-quarters years after the thoracoplasty the patient was readmitted to this hospital because of fever and pain in the right side of the chest. His wound had reopened spontaneously. Bone bridges together with the portions of two ribs above them were excised and two months later further rib resections were performed. Seven months after the last procedure the wound was healed. Six and one quarter years after the original operation the scar adherent to the pleura broke down, and at this time a plastic operation on the soft tissues was successful in closing the wound. In December 1937 clinical (fig 2) and roentgen (fig 3-4) examinations revealed a dorsal curve to the right of 97 degrees, with the apex at the tenth dorsal vertebra. There were dorsal kyphosis and an acute lumbosacral angle. The ribs on the right side were oblique and those on the left side horizontal. There was marked rotation of the vertebral bodies.

The exercise tolerance test showed moderate dyspnea and slight fatigue. The venous pressure was 6 cm, the vital capacity ¹² 1200 cc and the circulation time thirteen seconds, the results of all the tests except that for vital capacity being within normal limits. The scoliosis was so extreme that it caused dysphagia due to displacement of the esophagus as demonstrated by roentgen studies after ingestion of a barium sulfate meal (fig 3B).

Summary of Case 1—The patient had a slight postempyemic curve (5 degrees) with the concavity on the diseased side. Nine months after a thoracoplasty this had been transformed into marked scoliosis in the opposite direction, convex on the side of operation. In the next six years the curvature progressed to 97 degrees.

CASE 2—S. L., a girl aged 14 years, was admitted to the hospital in 1936 with the following history:

At the age of 2½ years there was empyema on the right, the pus containing *Staphylococcus aureus*. This was drained through an intercostal incision. Four years later, when the patient was 6 years old the mother noticed a spinal curvature, which has been treated by braces and plaster casts ever since. Six months before admission to the Mount Sinai Hospital the patient had been admitted to another institution where drainage had been done for a recurrence of the empyema. Since that time the wound had remained open. There was marked scoliosis in the upper dorsal part of the spine visible on both clinical and roentgen examination, with the concavity on the side of the empyema. There was a draining sinus in the seventh space and dulness on percussion of the entire right side of the

¹² Flügstad, A. E. and Kollman, S. Vital Capacity and Muscle Study in One Hundred Cases of Scoliosis. *J. Bone & Joint Surg.* 10: 724, 1928.

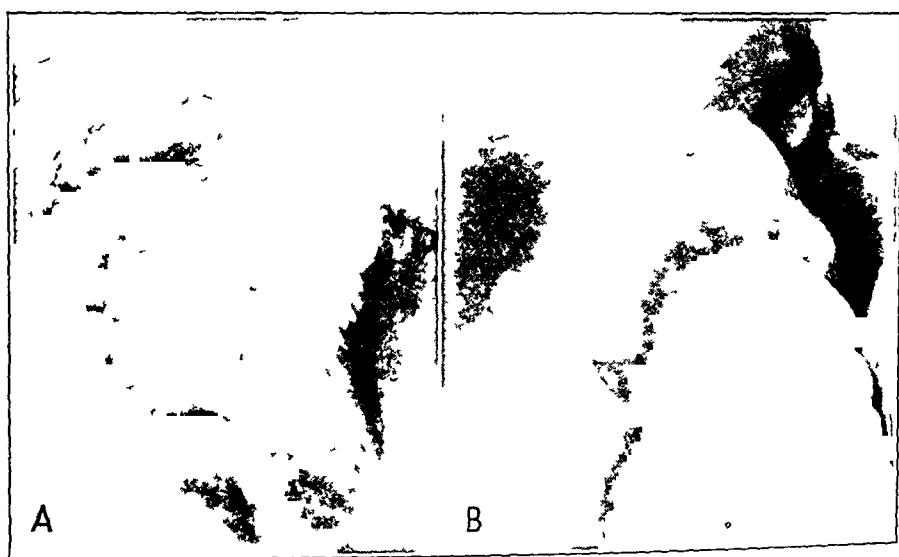


Fig 3 (case 1) —*A*, severe spinal curvature (97 degrees) with convexity to the side of the thoracoplasty *B*, displacement of the esophagus, demonstrated by roentgen studies after ingestion of a barium sulfate meal The condition produced dysphagia

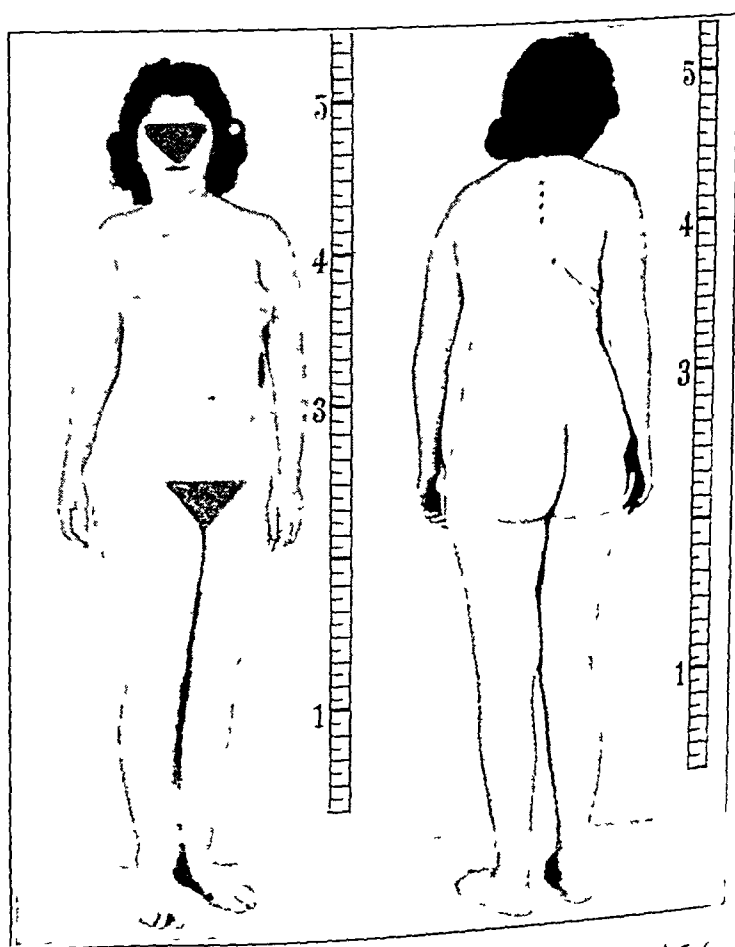


Fig 4 (case 2) —Appearance of the patient fifteen years after illness

chest. Roentgen examination showed that there had been a resection of the seventh, eighth and ninth ribs on the right side in the posterior axillary line, with bony bridging. Operation consisted of excision of a fused mass of bone at the old operative site together with thickened pleura and revealed extensive chronic empyema with a collapsed lung. The wound healed nine months after the operation, and a plaster jacket and later a brace were applied in an attempt to correct the spinal curvature. In January 1938 clinical (fig 4) and roentgen (fig 5) examination revealed thoracic scoliosis without rotation of the bodies with the apex at the sixth dorsal vertebra. The curve was severe (44 degrees) and had its concavity on the right, the side of the empyema.



Fig 5 (case 2).—Severe spinal curvature (44 degrees) concave to the side of the empyema.

Summary of Case 2.—The child was operated on at the age of $2\frac{1}{2}$ years for empyema on the right side, which was followed by scoliosis concave to the diseased side. Four years later this was severe enough to attract the mother's attention. Although treated by braces and jackets it progressed to 44 degrees. This was the only severe empyemic curve in our series.

Three patients presented slight curves. Two were patients with chronic empyema beginning at the age of 12 on whom multiple short rib resections had been performed. When observed eighteen years later both had high dorsal curves of 17 degrees and 12 degrees.

respectively, with the concavity on the side of the empyema and compensatory dorsolumbar curves in the opposite direction

The remaining patient, a boy, had chronic empyema beginning at the age of 4 years. A partial thoracoplasty was done at the age of 10 years. When observed four years later, he had a curve of 9 degrees with the convexity on the diseased side.

An analysis will now be made of the 60 cases in which empyema was not followed by lasting scoliosis. For purposes of analysis the cases

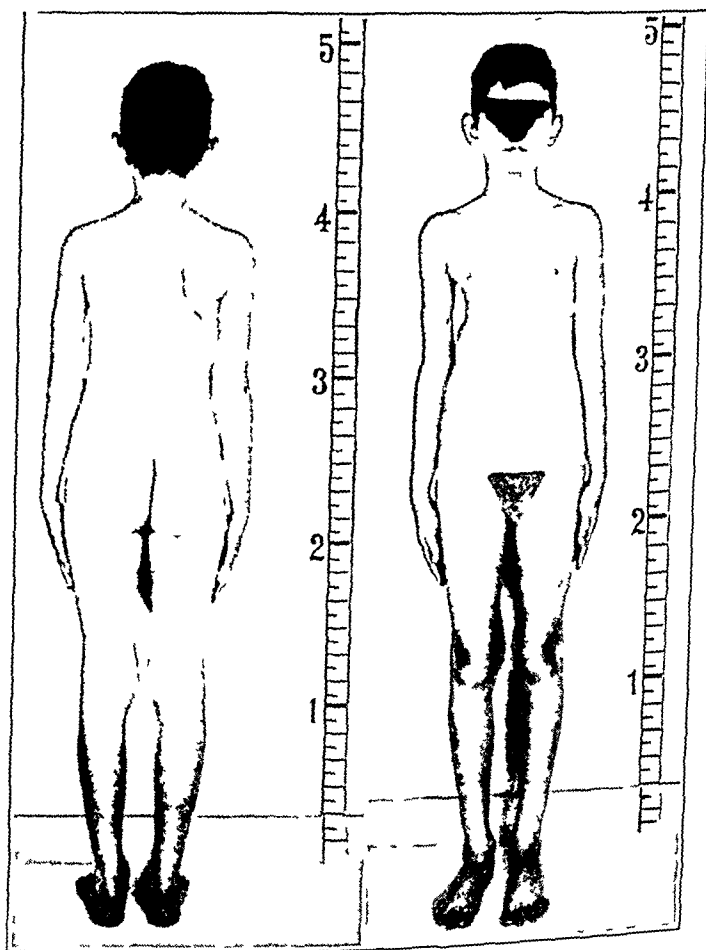


Fig 6—Patient showing no spinal curvature in spite of an extensive thoracoplasty for chronic empyema

are divided into groups according to the age of onset, and the patients in each age group are subdivided into those with acute and those with chronic empyema.

Four of the patients were infants under 1 year of age. Of these, 3 had acute empyema, in 2 a stab thoracotomy and in the other a small rib resection was done before healing occurred.

The fourth patient was of unusual interest because chronic empyema beginning in infancy and requiring extensive surgical treatment, includ-

ing a Keller¹³ thoracoplasty at the age of 8 years was not followed by scoliosis. When the child was observed three years later there was no evidence of a spinal curve (fig. 6).

In 24 patients the condition began between the ages of 1 and 5 years inclusive. In 22 it was acute and healed rapidly but in 2 it was chronic. In neither of these 2 did scoliosis develop in spite of multiple operations for chronic empyema.

In 12 patients the empyema began between the ages of 6 and 10 years. In 11 of these it was acute and was rapidly cured by surgical treatment, in the twelfth it became chronic. This patient in spite of extensive surgical treatment for chronic empyema did not have scoliosis.

In the age group from 11 to 20 years there were 2 patients with acute empyema and 1 in whom the empyema became chronic. In spite of extensive surgical procedures for chronic empyema beginning at the age of 17 (the patient was a girl) no scoliosis occurred.

In the group of patients 21 years of age or older there were 14 with acute and 4 with chronic empyema. In none of these was the empyema followed by scoliosis. We do not believe that an analysis of the observations on each patient is warranted, because the disease began after growth had ceased.

SUMMARY

This paper is based on a study of 65 patients with pyogenic non-tuberculous empyema who were operated on in the years of 1932 to 1936 inclusive in the surgical services of the Mount Sinai Hospital. This group includes all patients who returned in 1938 for examination of the spine.

Five patients showed clinical evidence of scoliosis, which was marked in 2. The most severe curve 97 degrees, followed a thoracoplasty at the age of 12 years for chronic empyema. The scoliosis was of the usual thoracoplasty pattern, with the convexity on the side of operation and with considerable rotation of the vertebral bodies. Treatment with various types of jackets was of no avail. The other severe scoliosis followed chronic empyema for which operation was first performed when the patient was 2 years of age. The curvature was noted four years later and progressed in spite of treatment with jackets and braces. The scoliosis was marked (44 degrees) at the time of admission, when the patient was 14 years of age. It was of the postempyemic type, with the concavity toward the diseased side and without rotation of the vertebral bodies. In the remaining 3 patients the curvature was slight, varying from 5 to 17 degrees. In 2 of these the scoliosis followed

¹³ Keller W. L. The Treatment of Chronic Empyema. *Ann. Surg.* 76: 549, 1922.

chronic empyema for which operation was performed when the patients were 12 years of age, the curvatures being of the postempyemic type previously described. A third patient had a thoracoplasty type of curvature after thoracoplasty for chronic empyema at the age of 10 years.

Sixty patients showed no evidence of scoliosis. The accompanying table gives the age at onset and the type of empyema in their cases.

Age at Onset and Type of Empyema in Patients Without Scoliosis

Age, Years	Number of Cases	Acute Empyema	Chronic Empyema
Under 1	4	3	1
1 to 5	24	22	2
6 to 10	12	11	1
11 to 20	2	2	0
Over 20	18	14	4

None of the 52 patients with acute empyema whose wounds healed permanently in the mean time of four months or less had persistent scoliosis.

Of 13 patients with chronic empyema requiring multiple operations, rib resections and excisions of the soft parts, persistent scoliosis developed in 5. These 5 patients were all in the group (9 patients) whose illness began at 12 years of age or under. In 2 of these the curvatures followed thoracoplasties, with a resultant thoracoplasty type of scoliosis, and in 3 they followed multiple rib resections, with a postempyemic type of curvature.

CONCLUSIONS

Persistent scoliosis is not a complication of acute empyema.

Persistent scoliosis frequently occurs as a complication after extensive operations on the thoracic cage for chronic empyema in children and surgeons should take prophylactic measures against its occurrence.

The reasons for the appearance or nonappearance of persistent scoliosis are not apparent.

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MULTIPLE MYELOMA

REVIEW OF FORTY CASES

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INCIDENCE

Multiple myeloma is a rare disease. Life insurance tables give its incidence as 0.03 per cent of all malignant growths or 3 per cent of all sarcomas of bone. In the American Registry of Bone Tumors its relative incidence is somewhat higher, in proportion to osteogenic sarcoma it is in the ratio of approximately 1 to 12, and to Ewing's sarcoma, of approximately 1 to 3. Of the 200 primary malignant tumors of bone seen at the University Hospital since 1925, 40 have been diagnosed as multiple myeloma—an incidence of 20 per cent. This is at marked variance with the figures usually given, the incidence of multiple myeloma at the Johns Hopkins Hospital being only 3 per cent of 400 sarcomas of bone. The 40 patients with multiple myeloma reported on here were encountered in a series of 298,546 patients admitted to the hospital, a ratio of 1 to 7,464.

GENERAL CONSIDERATIONS

Unlike osteogenic sarcoma and Ewing's tumor which occur principally in young persons, multiple myeloma is a disease of later life. Seventy-three per cent of the tumors in this series occurred from the fifth to the seventh decade inclusive. The average age at the time the diagnosis was made was 53 years with a range from 28 to 73 years. The tumor in the youngest patient was verified microscopically as typical plasmacytoma. This is significant because there are only 2 reported cases of multiple myeloma in an adult under 30 years of age, Moore¹ reported a case in which the patient was 27, and Haberfeld and Lord² a case in which the patient was 22.

From the Department of Surgery, the Orthopedic Service of Dr. Carl E. Bridgley, University Hospital.

¹ Moore S. Multiple Myelomata. *Radiology* 5:18 (July) 1925.

² Haberfeld W. and Lord C. Contribuição ao estudo anatômico e clínico do síndrome de Hodgkin e do mieloma. *Arch. brasil. de med.* 7:431, 1917. Geschickter and Copeland.³

The reported cases of myeloma in children have been collected by Geschickter and Copeland,³ and in each of these the diagnosis was open to serious question. Originally there was included in this series the case of a 15 year old boy who had multiple lesions with microscopic characteristics closely resembling those of myeloma. This case was dropped because ultimately a diagnosis of Ewing's endothelial myeloma was made.

Multiple myeloma occurs more frequently in males than in females. Of 40 patients, 25 were men, an incidence of 63 per cent.

There was a family history of some type of malignant growth in 31 per cent of cases. In 51 per cent there was no such history, and in the remaining 18 per cent it was not definitely established whether such growths had occurred.

Definite inquiry for a history of trauma elicited a negative response in 28 cases, or 70 per cent. Of the patients in the remaining 12 cases, 3 recalled an injury but in each instance it had occurred five or more years prior to the onset of symptoms, hence it is improbable that in these 3 cases there was an etiologic relation between the trauma and the development of myeloma. In 3 cases no information regarding trauma was available. In 2 cases a minor injury initiated the symptoms of myeloma, indicating that the trauma merely called attention to the underlying lesion. In only 4 cases was there a history of trauma antedating the onset of symptoms of myeloma by less than five years, the interval in these cases varying from five to twelve months. It seems justifiable to conclude from this series that trauma plays an insignificant role in the development of myeloma.

CLINICAL CHARACTERISTICS

There was no typical clinical history of multiple myeloma. However, an analysis of the symptoms furnished a few facts of considerable interest. As has been stated, the disease occurred relatively late in life, the average age being 53 years. Pain occurred in every instance. There was nothing diagnostic in the type of pain, its location or its duration. The average interval between onset and admission to the hospital was thirteen months, the shortest period being six weeks and the longest five years. The pain was variously described as dull, aching, rheumatic, neuritic and, in a few cases, sharp and lightning-like. In 53 per cent of the cases pain was referred to the back, most often to the lumbar region. Pain in the chest or over the ribs or the sternum occurred in 25 per cent of the cases. In 55 per cent there was pain in the extremities most often in the shoulders, hips and thighs. Pain in the lower extremities

3 Geschickter, C. F. and Copeland, M. M. *Tumors of Bone (Including the Jaws and Joints)*, revised ed. New York, American Journal of Cancer 1936.

ities frequently was of the radiating type often associated with pain low in the back. In 1 case the only symptom was a painful defect in the skull.

Geschickter and Copeland³ have pointed out that there is a typical course of pain in cases of multiple myeloma: a first stage, of intermittent, indefinite pains which become worse on motion or pressure, a second period, of aggravation with intense pain, a third period, of subsiding, intermittent pains, a fourth period, of relative freedom from pain with symptomatic relief, and a fifth and final stage, of recurrent, progressively intense pain proceeding to death. Only a few cases in our series could be fitted into this classification. However, the growth in more than 50 per cent ran a course characterized by three stages, namely, a period of onset, a single remission extending over a few weeks to several months and a final stage characterized by progression to the terminal event.

The appearance of tumor masses was one of the presenting symptoms in 13 cases, or 32 per cent of the total number. In 5 additional cases palpable tumors were found on physical examination, bringing the incidence up to 45 per cent. The most frequent sites of these tumefactions were the skull and the sternum. In 1 case the only symptom or sign of multiple myeloma on examination was a soft, tender defect in the skull, it was not until several months later that other lesions were demonstrable by the roentgen rays, in the spine, ribs and shoulder girdle. With this 1 exception the tumefactions in the skull were always multiple. Without exception the palpable tumors elsewhere were solitary. There were 5 cases of tumors of the skull, 5 of tumor of the sternum, 3 of tumor of the pelvis and 1 each of tumor of the orbit, the mandible, the spine, the scapula and the ribs. The tumors were tender, soft and exceedingly vascular. In 1 case there was a definite bruit, in another an attempt at removal of tissue for biopsy resulted in such a massive hemorrhage that the attempt had to be abandoned and the wound packed. The occasional observation of fluctuation in the size of a tumor may be explained on the basis of hemorrhage into the tumor with subsequent absorption of the hemorrhage.

At the time of admission to the hospital the majority of patients did not present the constitutional symptoms usually associated with malignant disease, namely, weakness, easy fatigability, anorexia, loss of weight and pallor. When such symptoms appeared the disease was usually well advanced.

The incidence of pathologic fracture in multiple myeloma is high. However, this finding varies with the stage at which the patient is seen. Since the tumor is bone destructive the longer the patients are followed

the higher the incidence becomes. Geschickter and Copeland³ found pathologic fractures in 62 per cent of patients with multiple myeloma as compared with 33 per cent of patients with metastatic carcinoma and 8 per cent of patients with osteogenic sarcoma. In the present series pathologic fracture was diagnosed in 23 per cent. The fractures occurred most frequently in the ribs and clavicles. Fracture of the upper end of the femur occurred in 5 and fracture of the humerus in 2. In 1 of these the fracture of the humerus was followed by healing. Union of fractures has been reported by Meyerding,⁴ Moore,¹ Bruce and others. Figure 1 shows a healed pathologic fracture of a rib.



Fig 1—Two views of the same rib, showing healing of a pathologic fracture secondary to multiple myeloma

The deformities produced by multiple myeloma are confined to the trunk and occasionally are found in the shoulder or in the pelvic girdle. In 7, or 18 per cent, of the patients there was a definite kyphosis, in 6 in the dorsal region and in 1 in the lumbar. Three of these patients had a localized gibbus due to collapse of a single vertebral body. In the majority of patients with spinal involvement there was exaggeration of the normal dorsal kyphosis. With the destruction of the vertebral bodies there was, of course, shortening of the trunk with approximation of the ribs to the brim of the pelvis. Deformities of the chest wall took the form of tumors of the sternum (12 per cent), of the ribs or of the

4 Meyerding, H. W. Multiple Myeloma, *Radiology* 5:132 (Aug) 1927

clavicles One patient had a large tumor located in the buttock, arising from the ilium Another had a marked deformity of the head due to a tumor of the skull (fig 2)

Involvement of the nervous system was found in 35 per cent of the patients The most common neurologic finding was paraplegia of the lower extremities, which occurred in 7 patients, or 18 per cent The paralysis was usually the flaccid type and was accompanied by sensory changes, with disturbances of control of the bowel and of the bladder Typical sciatica occurred in 4 patients In 1 patient there was radiculitis,

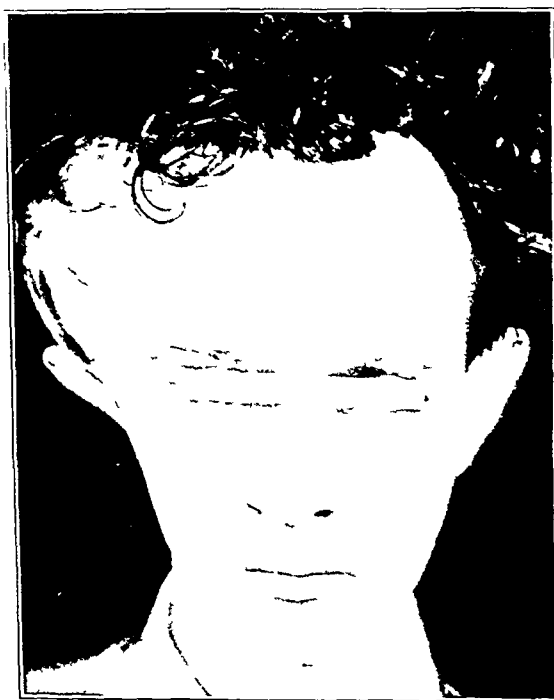


Fig 2—Unusual deformity of the head due to involvement of the skull in multiple myeloma

with sharp, severe shooting pains in both upper extremities In another there were similar pains encircling the thoracic cage

LOCATION OF LESIONS

Myeloma is almost invariably multiple In 3 patients in this series solitary involvement was found on the first admission, but subsequent studies showed multiple involvement in 2 of these, the other patient, with a solitary lesion of the right ilium which was diagnosed by biopsy, is living and well fifty-two months after admission with no other demon-

stable lesion. By roentgen examination the skull was found to be involved in 73 per cent of the patients, the spine in 70 per cent, the ribs in 68 per cent and the pelvis in 63 per cent. The skull and spine together were involved in 53 per cent, the skull, spine and ribs together, in 38 per cent, and the skull, spine, ribs and pelvis together, in 23 per cent. The shoulder girdle, including the scapulas and clavicles, was involved in 40 per cent, the humerus in 43 per cent and the femur in 48 per cent. The humerus and femur were uniformly invaded in their proximal portion. The ulna was involved in 2 patients, the tibia in 2, the radius in 1 and the fibula in 1. It will be noted that the sites of predilection were those where there is persistent formation of blood in the adult. In no instance was involvement of the hand or foot demonstrated. However, Meyerdig¹ has shown a roentgenogram of a patient in whom all of the bones of the hand were involved.

ROENTGEN FINDINGS

As usually described, the roentgen findings in cases of multiple myeloma are characteristic. These characteristic features were observed in 24 cases in this series, or 60 per cent. The individual lesions were seen as definitely circumscribed areas of decreased density, varying from a few millimeters to several centimeters in diameter. The smaller areas appeared as punched-out lesions, the larger ones, as a complete melting away of bone. Figure 3 shows typical lesions of multiple myeloma in the skull. There was no reaction about these areas of destruction. Being definitely tumors of marrow, the lesions appeared roentgenologically as typically central.

In the remaining 16 cases, or 40 per cent, it was impossible to make a definite diagnosis of multiple myeloma by roentgen examination. In several cases there was evidence of osseous reaction about the individual lesions, a finding which is more typical of metastatic malignant tumor than of multiple myeloma and has been used as a distinguishing feature. In the 3 cases of initial solitary involvement the lesions could not be distinguished roentgenographically from the changes produced by osteoporosis of the spine with wedging of the individual vertebrae, such as has been described in reports of osteomalacic diseases associated with abnormal calcium metabolism and with hyperparathyroidism. Occasionally they appeared mottled owing to the coalescence of several areas of destruction. Some of the larger lesions gave the appearance of being expansile, a thin shell remaining and enclosing the area of destruction. However, as Moore¹ has pointed out, this seeming expansion is not actual distention of the bone but the result of internal resorption with external deposition of bone. That bone formation can occur in multiple myeloma has been proved by the occasional healing of pathologic fractures as well as by microscopic examination.

LABORATORY FEATURES

The outstanding laboratory finding in cases of multiple myeloma is the presence of Bence Jones bodies in the urine. The high incidence (80 per cent) reported in the older literature has not been confirmed in recent publications. In the present series studies for Bence Jones bodies were made in 34 cases with positive findings in 17, or 50 per cent. In several cases in which the findings were positive repeated examinations of the urine were necessary. In 1 case four successive

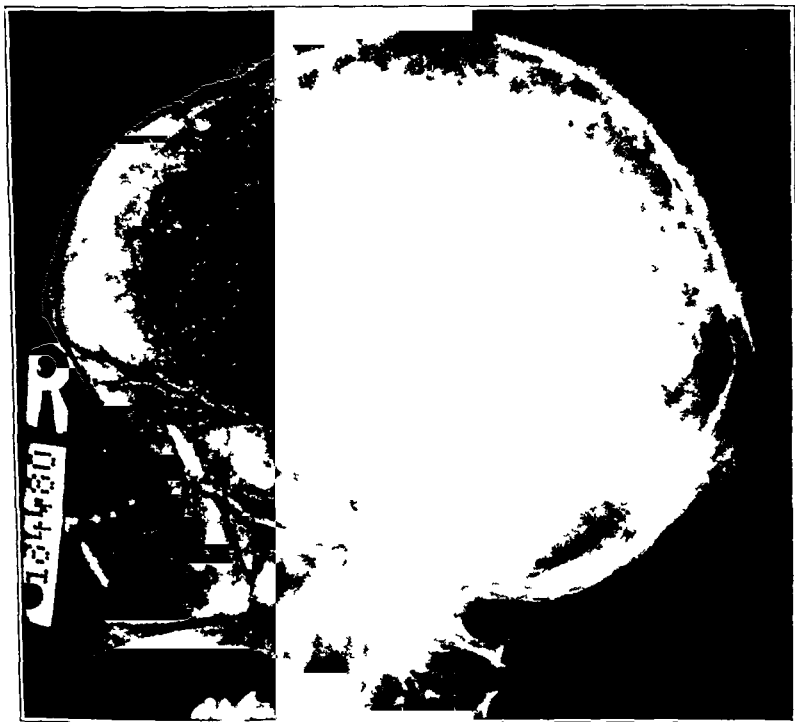


Fig 3—Roentgenogram showing the typical lesions of multiple myeloma in the skull. There are multiple punched-out areas of destruction with no evidence of osseous reaction about them.

tests gave negative results, whereas the fifth showed the typical cloudy white precipitate between the temperatures of 50 and 60 C, which cleared up on boiling. It is evident from this that Bence Jones bodies are often present only intermittently. As the disease progresses toward the final stage the finding tends to become constant.

Just as the absence of Bence Jones bodies in the urine does not rule out multiple myeloma, so their presence is not pathognomonic of the disease. They have been found associated with metastatic tumors of

bone, senile osteomalacia, polyfibrocystic disease of bone, caries of the spine and leukemia (both of the lymphatic and of the myelogenous type) It will be noted that all of these conditions involve the "red marrow bones" The exact source and significance of the albuminoid substance is not known The fact that it is found in the urine does not mean that it is due to renal damage, as was proved by autopsy on a patient in whom there was no evidence of renal damage but who showed Bence Jones proteinuria during life

Determinations of serum calcium and phosphorus were made in one third of the cases In only 2 cases were there definitely abnormal findings, in 1 there was a serum calcium content of 13.5 mg and a serum phosphorus content of 7.5 mg per hundred cubic centimeters, in the other there was a serum calcium content of 13.8 mg and a serum phosphorus content of 3.9 mg per hundred cubic centimeters

All types of blood pictures have been reported in cases of multiple myeloma In this series the most constant finding was secondary anemia, which was mild in 38 per cent, moderate in 13 per cent and severe in 23 per cent of cases The primary anemia which has been reported occasionally and has been supposed to be due to displacement of hemopoietic tissue by tumor elements was not found In 4 cases there was leukopenia on the patient's first admission to the hospital In 3 cases there was leukocytosis, the leukocyte counts being 11,600, 12,500 and 15,500 per cubic millimeter respectively Circulating plasma cells were found in 3 cases "Blast" cells either of the lymphocytic or of the myelocytic series were found in 3 cases How closely multiple myeloma may simulate leukemia is shown by the following case

C. S., a 41 year old man, had noted pain in the back, head and legs for four months Three weeks before admission he had had repeated epistaxes for which repeated transfusions were necessary He was admitted to the hospital in coma Roentgen examination showed destructive lesions of the spine, the skull and the ribs No Bence Jones bodies were found in the urine Studies of the blood showed a hemoglobin content of 28 per cent, the red cell count was 1,810,000 and the white cell count 15,500 per cubic millimeter, the differential cell count showed myeloblasts 4 per cent, myelocytes 6 per cent, metamyelocytes 11 per cent, young polymorphonuclear leukocytes 32 per cent, adult polymorphonuclear leukocytes 25 per cent, eosinophils 3 per cent, large lymphocytes 12 per cent, small lymphocytes 5 per cent and monocytes 2 per cent A clinical diagnosis of leukemia was made The patient died a few days after admission At autopsy the diagnosis was multiple myeloma of the mature plasmacytoma type

PATHOLOGIC CHARACTERISTICS

In 23 cases, or 58 per cent, the diagnosis of multiple myeloma was confirmed by pathologic study Grossly the tumors were surrounded by a thin shell of bone which could be cut easily with a knife The tumor tissue was dark red or grayish red, depending on its vascularity

One tumor was virtually black, owing to the presence of old hemorrhage. As has been noted the fluctuation occasionally seen in the size of a tumor was probably due to hemorrhage into the tumor with subsequent absorption.

Microscopically the growths in 18 of the 23 cases, or 78 per cent, were diagnosed as plasmacytoma. The typical picture was that of closely packed round cells occurring in solid sheets with little or no intercellular stroma. The tumor tissue was rich in blood vessels, which

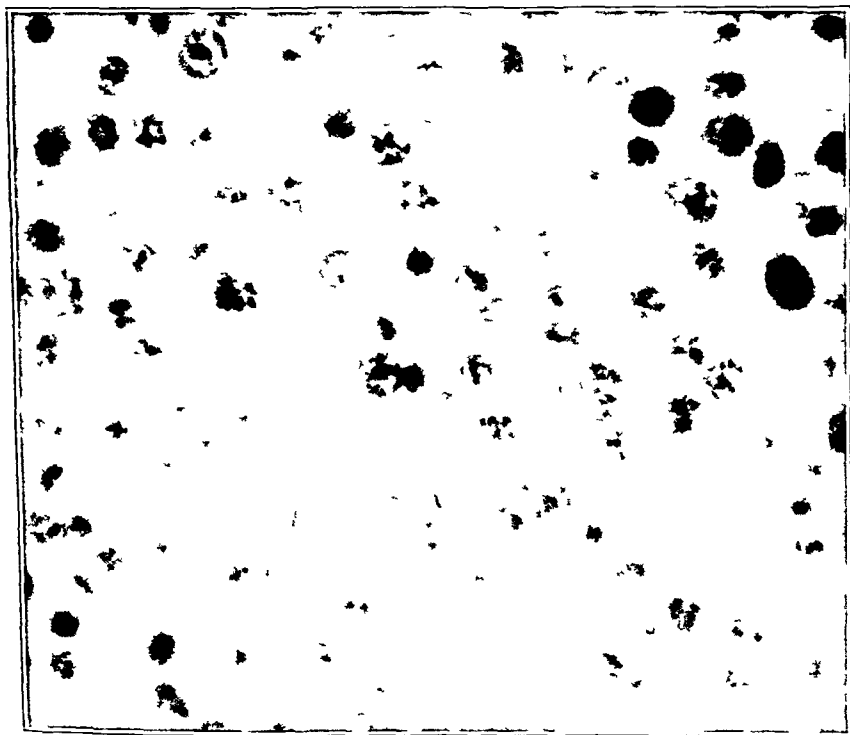


Fig 4—High power photomicrograph of a typical myeloma, the so-called plasmacytoma. The cells occur in solid sheets and each has an eccentric nucleus about half the diameter of the cell. Within the nucleus there is a spokelike arrangement of the chromatin. There is practically no intercellular substance.

were thin walled and lined with a single layer of endothelium. The individual tumor cells were uniform in appearance, with an eccentric nucleus about half the diameter of the cell, abundant eosinophilic cytoplasm and a spokelike arrangement of the chromatin within the nucleus (fig 1). The nucleus had a well defined membrane within which was a nucleolus. Scattered among these cells in almost every case were smaller cells a little more than half the diameter of the others with scant

cytoplasm, somewhat resembling lymphocytes. Whether these cells have the same derivation as the plasma-like cells has not been determined.

In 2 cases the type of cell was identical with that observed in Ewing's sarcoma. It was about 7 to 9 microns in diameter, had a deeply staining round or oval nucleus, scanty pink-staining cytoplasm and no definite arrangement of the chromatin in the nucleus. The microscopic diagnosis in these cases was round cell sarcoma, and the diagnosis of multiple myeloma was made on characteristic clinical features.

In 1 case a diagnosis of myeloblastic myeloma was made, the cells closely resembling those of the myelocytic series. In the remaining 2 cases an unqualified diagnosis of multiple myeloma had been made previously, and the sections were not available for further examination when this study was made.

Autopsy was performed in 14 cases, or 35 per cent. In 3 of the 14 cases autopsy was done elsewhere, so that the material was not available for study. Of the remaining 11 cases, there were 6 in which myelomatous involvement of the soft tissues occurred. In the first of these 6 cases there was infiltration of the liver, spleen, lymph nodes and kidneys, with vicarious hemopoiesis in the liver, kidneys and lymph nodes. In the second case there was retroperitoneal dissemination with massive infiltration of the pancreas and invasion of the rectum, seminal vesicles, prostate and bladder. In the third case there was infiltration of the meninges, liver, kidneys and periaortic lymph nodes. In the fourth there was infiltration of the dura (from the calvarium), in the fifth, of the thyroid, and in the last case, of the liver. Thus it is evident that multiple myeloma is a disease which is not limited to the skeleton. Clinically the infiltration of extraskkeletal tissues is not often noted. Metastases to the lung are unusual, contrary to the finding in other forms of bone sarcoma. In only 1 case were pulmonary metastases found, they were diagnosed by roentgen examination.

The type of renal involvement observed at autopsy was not characteristic of multiple myeloma. In 2 cases there was infiltration of the kidneys by the malignant tumor tissue. Of the 11 cases in which sections of the kidney were reviewed arteriolosclerotic nephropathy of varying severity was observed in 8, simple atrophy and calcification of the tubules in 2 and hydronephrotic atrophy in 1. The glomeruli showed relatively slight changes, usually hyaline thickening of the basement membrane or fibrosis of a few scattered glomeruli. Tubular casts were present in 5 cases. There was no evident correlation between the type or severity of renal damage and the appearance of Bence Jones protein in the urine. As has been pointed out by Bell,⁵ clinical obser-

5 Bell, E. T. Renal Lesions Associated with Multiple Myeloma, *Arch. Path. & Lab. Med.* 9: 393 (July) 1933.

vations and animal experiments have shown that apparently Bence Jones protein may pass through normal kidneys

Bell⁶ has also demonstrated a more or less characteristic effect of multiple myeloma on the kidneys. There is formation of tubular casts of Bence Jones protein that obstruct the tubules and cause proximal tubular atrophy. When large numbers of tubules are obstructed, extensive atrophy of the cortex and renal insufficiency ensue. A comparable picture was found in only 1 case in this series.

TREATMENT

Since the prognosis for life is hopeless, it is customary to indicate that treatment is chiefly symptomatic and that in certain cases roentgen therapy may be helpful in controlling pain. In the present series, however, two things deserve special mention, namely, the effect of roentgen therapy on the duration of life and the treatment of paraplegia.

It is generally recognized that the use of roentgen therapy for multiple myeloma results in symptomatic improvement with relief of pain. Of the 40 patients studied, 23, or 58 per cent, received roentgen therapy. Seventy-eight per cent of these had definite relief from pain, as to the remainder, no information regarding this point was available. As administered by the department of roentgenology, the doses of radiation were equivalent to single doses of 600 roentgens (r) to each area. In a number of instances the radiation was fractionated into doses of 200 r each. The factors of treatment were a filter of 0.9 mm of copper (a half value layer) with the tube at a distance of 50 cm from the skin and an intensity of 30 to 50 r per minute. The treated areas varied from 100 to 400 sq. cm.

Symptomatic treatment without roentgen irradiation was administered to 17 patients. In this group the average duration of life after admission to the hospital was six months. On the other hand, the group which received roentgen therapy had an average duration of life after admission of twenty-three months. The latter group includes 5 patients who are still living at the time of this report, so that the difference in the average periods of survival will become greater until all the patients have died.

In the symptomatically treated group 4 patients died within a few days after admission. When these 4 are omitted from the comparison, the average period of survival after admission was eight months for the 13 patients who received symptomatic treatment. Further study showed that these 13 patients were seen, on the average, four months later in the course of the disease than were the group treated by roentgen irradiation. By eliminating the differences due to the stage at which treatment was started, it was found that the patients treated with

roentgen rays lived twenty-three months after admission and treatment, as compared with a twelve month survival for the patients who did not receive roentgen therapy

In 1933 Jacox and Kahn⁶ reported on 2 patients who had multiple myeloma with involvement of the spinal cord and who were treated by laminectomy and roentgen therapy. At the time of their report both patients were free from symptoms and working daily. One of them died on Aug 9, 1936, eight years and six months after admission (nine years and six months after the onset of symptoms). The other died of pneumonia on April 3, 1934, thirteen months after admission, after a complete recovery from motor paralysis of the lower extremities and sensory paralysis below the fifth dorsal segment.

Since 1933, 3 additional patients have been treated by laminectomy at the University Hospital.

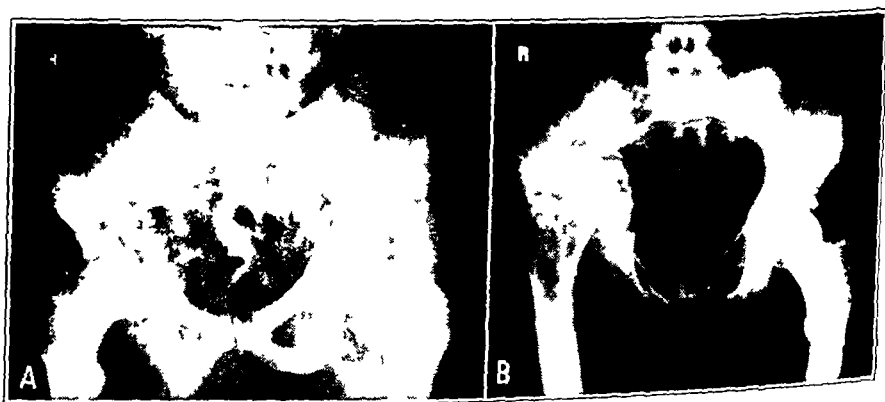


Fig 5—Solitary myeloma with the pathologic characteristics of plasmacytoma. A, melting away of a portion of the acetabulum and ilium. The patient was given roentgen therapy. B, result forty-nine months later. There is evidence of healing and intrapelvic protrusion of the head of the femur. The patient is living and well fifty-two months after the institution of treatment.

G. H., a 64 year old man, had complete motor paralysis of both lower extremities of four weeks' duration, with sensory paralysis beginning at the level of the fourth dorsal segment and involvement of the bladder. Roentgen examination showed involvement of the fourth dorsal vertebra and of the ribs. On April 8, 1935 a decompressive laminectomy was done, with partial excision of a growth. A red gelatinous tumor. Microscopically the lesion was a plasmacytoma. There was a gradual return of motor and sensory function, but the patient died on the fourth postoperative day of a massive facial infection and pneumonia.

M. W., a 62 year old man, was admitted to the University Hospital on Feb 26, 1934, the chief complaint being paralysis of the lower extremities. During the two months prior to admission there had been pain between the scapulae.

⁶ Jacox, H. W., and Kahn, E. A. Multiple Myeloma with Spinal Cord Involvement, *Am J Roentgenol* 30 201 (Aug) 1933.

and in the left upper anterior part of the chest. Ten days prior to admission the patient noted numbness from the waist down, associated with motor paralysis of the lower extremities, during this same interval there was complete retention of urine, and daily catheterizations were necessary. Examination revealed sensory paralysis beginning at the level of the second dorsal segment and spastic paralysis of the lower extremities. Roentgen examination showed gross destruction of the second dorsal vertebra. On February 28 a decompressive laminectomy was done, with partial excision of a grayish soft vascular tumor projecting into the spinal canal from the second dorsal vertebra. Three weeks later roentgen therapy was



Fig 6—Lateral view of the spine, showing complete disappearance of the third lumbar vertebra. The small flake of calcium between the second and the fourth lumbar vertebra is all that remains of the third lumbar vertebra. There is posterior displacement of the second lumbar vertebra on the fourth. A laminectomy had been performed for paraplegia, followed by roentgen therapy. The pathologic diagnosis was plasmacytoma.

started, a total dose of 1,600 r being given over a period of seven weeks. Immediately after the operation the paraplegia began to improve. One month after the operation the patient was able to walk with crutches, two months later he could walk with a cane, and thereafter he was able to resume work. The vesical difficulty disappeared completely. This patient died on July 29, 1938, four years

and five months after laminectomy, of lobar pneumonia, with no recurrence of the paraplegia or of the associated vesical symptoms. Autopsy confirmed the diagnosis of multiple myeloma.

U K, a 60 year old woman, complained of pain in the back of twenty six months' duration. During the four weeks previous to admission she noted weakness of both lower extremities, inability to walk, sensory paralysis beginning at the level of the first lumbar segment and considerable difficulty in micturition. Roentgen examination showed involvement of only the eleventh dorsal vertebra. A laminectomy was done on July 29, 1938, and a grayish soft tumor was encountered projecting from the body of the eleventh dorsal vertebra. Partial resection of the tumor was carried out, with removal of the laminae of the tenth to the twelfth dorsal vertebrae. Microscopic examination showed a plasmacytoma. One week after operation the patient was given a course of roentgen therapy, the total dose being 1,200 r. One month later she was discharged with complete sensory recovery, normal function of the bladder and of the bowel, and increasing motor power in the lower extremities. One month later she had resumed walking. On November 30, four months after operation, she reported herself as well.

With the exception of the 1 patient who died postoperatively of an unrelated infection, laminectomy followed by roentgen therapy was eminently successful in these cases of involvement of the spinal cord. Dr. E. A. Kahn has called attention to the fact that in the presence of severe compression of the cord, laminectomy should always be done before roentgen therapy is given. This permits the establishment of a positive diagnosis and prevents further damage to the cord by swelling subsequent to irradiation.

PROGNOSIS

Multiple myeloma is invariably fatal, there being no permanent cure on record in a case in which the diagnosis was proved. Geschichter and Copeland stated that the average duration of the disease is two years and that the longest duration of the disease in any case proved to be one of multiple myeloma was five and one-half years. They stated further that the duration of the disease appears to be uninfluenced by treatment.

In this series 35 of the 40 patients have died, with an average duration of the disease from onset of symptoms until death of twenty-seven months. The average period from admission to death for these 35 patients was fourteen months. Of the 5 living patients, 1 is living well fifty-nine months after the onset of symptoms, 2 are living with evidence of improvement at twenty-eight and seventy-two months respectively, and 2 are living with evidence of progression of the disease at thirteen and forty-three months, respectively. The average duration of the disease in the living patients is forty-three months. The average duration in the entire series, living and dead, from onset until death or date of writing, is twenty-eight months, from admission to death or date of writing it is fifteen months. Obviously, the average will increase until all the patients have died.

Although a five year period of survival is considered unusual for a patient with multiple myeloma, 5 patients in this series or 12.5 per cent, lived longer than five years. Four of these died after surviving one hundred and seventy-two, one hundred and seventy-four, seventy-eight and sixty-one months, respectively, from the onset of symptoms until death. One patient is living with evidence of improvement after seventy-two months. As has been noted, 1 patient is living and well fifty-nine months after the onset of symptoms. In all of these cases the diagnosis was proved by microscopic examination except in the 2 in which the patients survived for seventy-eight and seventy-two months, respectively. These 2 had typical roentgen characteristics of multiple myeloma with Bence Jones proteinuria.

The patient who lived fourteen years and four months was a 49 year old woman who was admitted to the University Hospital on Oct. 1, 1928, complaining of pain in the left hip of five years' duration. Roentgen examination on admission showed destructive lesions in the left ilium and in the left femur. On October 20 a biopsy of material from the left ilium was done, which showed a myeloma of the plasma cell type. The patient was treated by roentgen irradiation and was discharged as improved. Subsequently she had destructive lesions in the skull, clavicle, scapula, ribs, spine, pubis and right humerus. Bence Jones protein, which had been absent from the urine on the first admission, was observed. In 1931 roentgen therapy was resumed, and it was given at intervals to the time of death, always with symptomatic improvement. In 1934 a biopsy was done elsewhere of material from a lesion of one of the ribs, which was also reported as myeloma. The patient died on Feb. 4, 1938, almost ten years after the first admission.

The patient who lived nine and one-half years was the one described in the first case reported by Jacob and Kahn. Treatment was by laminectomy and roentgen irradiation.

An attempt was made to evaluate the various factors which might influence the prognosis of multiple myeloma. The cases were divided on the basis of duration of symptoms previous to admission into three groups: group 1, duration of symptoms up to six months; group 2, duration of symptoms from six to twelve months; group 3, duration of symptoms over twelve months. In the first group, which comprised 14 cases, the average survival period was thirteen months after admission to the hospital. In the second group, which comprised 20 cases, the average survival period was sixteen months after admission. In the third group, which comprised 6 cases, the average survival period was twenty-seven months. From this it would seem that early diagnosis is of no benefit to the patient. Perhaps the proper explanation is that the more

⁷ This case is to be reported in a separate publication.

rapidly lethal the malignant process is, the more quickly it drives the patient to his physician because of the severity of the symptoms

The average age of the patients in this series was 53 years. The average total duration of the disease in the 18 patients under 53 years of age was thirty-five months, in the 22 patients over 53 years of age the average total duration of the disease was twenty-two months. The 2 youngest patients in this series, aged 28 and 32 years, respectively, are living with no evidence of progression of the disease at fifty-nine and seventy-two months, respectively, after the onset of symptoms. The conclusion from this series is that the younger the patient the better the prognosis in terms of the period of survival.

Three patients presented themselves with solitary lesions on the first admission. Two of these subsequently had multiple lesions. The first lived nine years and six months after the onset of symptoms, the second lived four years and seven months. The other patient is living and well fifty-nine months after the onset of symptoms, with no evidence of multiple lesions. To date the average total duration of the disease in these 3 cases is seventy-six months, as compared with the average total duration of twenty-four months in the remainder of the series.

The effect of treatment on the prognosis of multiple myeloma has been discussed in the section on roentgen therapy. The patients who received roentgen therapy lived on the average twice as long as those who did not receive it. Of the 5 patients in whom the total duration of the disease was over five years, 3 received roentgen therapy and two did not. The 2 who were not treated died one month and eighteen months, respectively, after admission. Each of the other 3 lived more than five years after admission, the average period from admission until death being eighty-seven months. It appears that roentgen therapy prolongs life in addition to controlling pain.

SUMMARY AND CONCLUSIONS

Multiple myeloma is a rare disease. It is a disease of middle and late life, the average age of the patients in this series being 53 years. It occurs almost twice as frequently in men as in women. Etiologically it is not related to trauma. Its chief symptom is pain, which may occur in any location and is not in any way characteristic except that there is usually a single period of remission. Palpable soft tumors are found in one half of the patients, usually on the skull or on the trunk. Pathologic fractures are common. Deformities of the thoracic cage and of the spine are not unusual. Paraplegia and nerve involvement referable to the spinal cord constitute frequent complications. Multiple myeloma occurs most frequently in the skull, spine, ribs and pelvis, in that order. Solitary lesions are rare and usually become multiple before death.

Roentgen examination shows multiple punched-out areas of osseous destruction with no evidence of osseous reaction. The laboratory findings show secondary anemia of varying severity and, in one half of the cases, Bence Jones protein in the urine. Microscopically the lesions show masses of round cells closely resembling plasma cells, with little or no intercellular substance. Autopsy reveals that in one half of the cases the soft tissues, particularly the liver, spleen and kidneys, are invaded by myeloma. The renal findings at autopsy are not characteristic, arteriolosclerotic nephropathy being present in most cases. Treatment in the past has been chiefly symptomatic, but roentgen therapy gives relief from pain and prolongs life. Laminectomy and decompression of the spinal cord are indicated in cases of paraplegia due to multiple myeloma. Multiple myeloma is invariably fatal, the average duration of the disease from the onset of symptoms until death being two and one-half years. Survival for five years is an occasional occurrence. The longest period of survival on record in a proved case is fourteen years and four months. The prognosis is more favorable for relatively young patients and for those with initial solitary involvement. The prognosis is favorably influenced by roentgen therapy and, in cases of paraplegia, by decompressive laminectomy.

Assistance in the compilation of this paper was furnished by Dr Carl V Weller, professor of pathology, and Dr Fred I Hodges, professor of roentgenology, and their respective staffs.

CAUSAL SIGNIFICANCE TO TRAUMATIC OSSIFICATION OF THE FIBROCARILAGE IN TENDON INSERTIONS

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Growths of bone tissue in muscles and in their tendinous insertions after trauma in muscle tissue about joints after dislocations or in soft tissues about a simple fracture of a bone or after a minor injury commonly are given such designations as traumatic myositis ossificans, parosteal callus or some other appropriately descriptive term. Summaries of the data on such growths have been written by Fay,¹ Painter,² Lewis,³ Carey,⁴ Gruca,⁵ von Dittich,⁶ Goto,⁷ Geschickter⁸ and others. All these reviews have emphasized trauma as the initiating factor. No age group is immune, but the incidence is greatest in young men. Fay stated that this indicates merely the frequency of trauma in a group leading an active life. The usual sites of these traumatic osseous growths are those exposed to injury in occupation, avocation or accident. According

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From the Henry Baird Favill Laboratory of St. Luke's Hospital

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3 Lewis, D. Myositis Ossificans, *J A M A* **80** 1281 (May 5) 1923

4 Carey, E. J. Multiple Bilateral Traumatic Parosteal Bone and Callus Formations of the Femurs and Left Innominate Bone, *Arch Surg* **8** 592 (March) 1924

5 Gruca, A. Myositis Ossificans Circumscripta, *Ann Surg* **82** 883 192

6 von Dittich, K. Beitrag zur Lehre von circumscriperten traumatischen Muskelverknöcherung und zur Frage der Metaplasia, *Virchows Arch Anat* **260** 436, 1926

7 Goto, S. Zur Kenntnis der sogenannten Myositis ossificans, *Arch Chir* **187** 781, 1937

8 Geschickter, C., and Maseritz, I. H. Myositis Ossificans, *J Bone & J Surg* **20** 661, 1938

to Cahier,⁹ three fifths of the bone formations in muscle have no attachment to the adjacent bone, the remainder are connected with it by a pedicle

The theories compiled by Carey include practically all those which have been offered in explanation of these intramuscular growths of bone. They are (1) the hemic theory, which assumes the transformation of an organized hemorrhage into cartilage and bone, (2) the theory of proliferation of aberrant sesamoid bone tissue following trauma, (3) the theory of growth of detached flaps of periosteum into bone, (4) the theory of dissemination of osteogenic cells and proliferation through a tear of the limiting periosteum, (5) the theory of hematogenous infectious myositis, (6) the theory of the escape of synovia into the soft tissues with organization, (7) the theory of metaplasia of intramuscular connective tissue into bone, (8) the theory of combined metaplastic and periosteal tissue growth and (9) the theory of an individual diathesis or dyscrasia. Pertinent objections confront these explanations. There is little evidence that the bone growths are neoplastic, although pathologists sometimes have mistaken the tissues for sarcoma. Factors (other than the immediate trauma) influencing the development of these bone tissues, according to Wagner¹⁰ are a shift to alkalinity of the tissue fluids, the growth of connective tissue cells and the activity of an enzyme that splits phosphoric acid from organic compounds.

The clinical course of traumatic ossification has been arranged into three stages.¹¹ At first the symptoms of trauma to the tissues are dominant, but the disability produced by the injury does not subside. After the second week pain reappears, the local swelling increases and the tissues become indurated. In the third or fourth week roentgenograms disclose a density in the soft tissues, which gradually assumes the characteristics of bone. As a rule there is no fever.

Histologic examination in the first stage demonstrates acute exudative inflammation of the tissues, edema and hemorrhage, the immediate sequelae of the trauma. Later there is scarlike connective tissue or granulation tissue with masses of bone and cartilage in varying amounts and residue of skeletal muscle. Gruca stated that the plates of bone arise directly from the connective tissue or indirectly from the connective tissue through a cartilaginous stage. The skeletal muscle fibers have no active part.

⁹ Cahier, L. Sur les myostéomes traumatiques particulièrement sur leur pathogénie et leur traitement opératoire. *Rev. de chir.* **29** 356, 1904.

¹⁰ Wagner W. Beitrag zur Behandlung der Myositis ossificans circumscripta. *Arch. f. klin. Chir.* **172** 543, 1933.

¹¹ Heidrich L. Röntgenbestrahlung bei der Myositis ossificans circumscripta, *Arch. f. klin. Chir.* **170** 256, 1932. Gruca.

A number of specimens of such intramuscular bone tissue in various stages have been encountered in routine examinations of surgical material at St. Luke's Hospital

REPORT OF CASES

CASE 1—A white man aged 35 had noticed for a year a painless mass in the muscles of the calf of his right leg and a similar but larger mass above the first for about two months. They had not increased appreciably in size. The only relevant injuries recalled were several blows on the muscle of the calf with a bowling ball within the past four years. On Jan 4, 1932, the two pieces of hard tissue, measuring respectively 5.5 by 3.5 by 1 cm., and 4.5 by 2.5 by 1 cm., were removed by Dr. H. E. Jones. Seventeen months later another mass, 3 by 3 by 1.5 cm., was removed from the medial portion of the belly of the right gastrocnemius muscle. This had been present for a few months in the old scar.

The tissue removed on Jan 4, 1932 contained differentiated lamellar bone. The narrow, compact trabeculae enclosed wide marrow spaces filled with fat. A thin fibrous capsule along the margins contained atrophied muscle fibers. Cartilaginous tissue was not present in the portions examined. The tissue removed on May 31, 1933 had less differentiated bone. Bone trabeculae were embedded in dense fibrous tissue that included atrophied and unchanged skeletal muscle fibers. Peripheral portions of the trabeculae had lamellar bone, and irregular regions near the centers were differentiated incompletely and contained basophilic granular material.

CASE 2—A mass of fibrous, muscle and bone tissue 2 by 1.5 by 1.4 cm was removed from the muscle tissues anteriorly near the center of the upper part of the right arm of a man aged 53 by Drs. H. E. Mock and J. D. Ellis. A matrix of fibrous stroma had trabeculae of compact bone. Some trabeculae merged into irregular masses of hyaline cartilage with large lacunae (fig. 1A). The associated dense scar tissue contained atrophied skeletal muscle fibers.

CASE 3—The lower third of the left thigh of a Negro aged 40 was bruised on March 4, 1925 by a heavy iron casting. He was incapacitated six weeks because of the painful swelling. The inflammation subsided, but a hard mass remained. On June 2 Dr. C. W. Hopkins removed soft, porous bone tissue. It was broken into small pieces. Thirty-five to fifty of these, with attached muscle and fibrous tissues, forming a mass 9 by 8 by 2 cm. which weighed 39 Gm., were submitted for routine examination.

Trabeculae of bone were embedded in edematous fibrous tissue with and without skeletal muscle fibers. Some of the bone tissue had a lamellar structure, some had a granular or hyaline matrix. These at suitable levels were continuous into hyaline cartilage with a fibrocartilage margin.

CASE 4—A white man aged 39 fell on Jan 27, 1929, dislocating his left elbow. There was no fracture, but for two months he had a swelling in the left elbow fossa. Flexion was limited. On August 6 Dr. W. F. Lyon removed a piece of bone 7.3 by 3.5 by 2 cm. that extended from the ulna into the biceps muscle. The histologic preparations contained trabeculae of differentiated bone and wide marrow spaces with fat and edematous fibrous tissue.

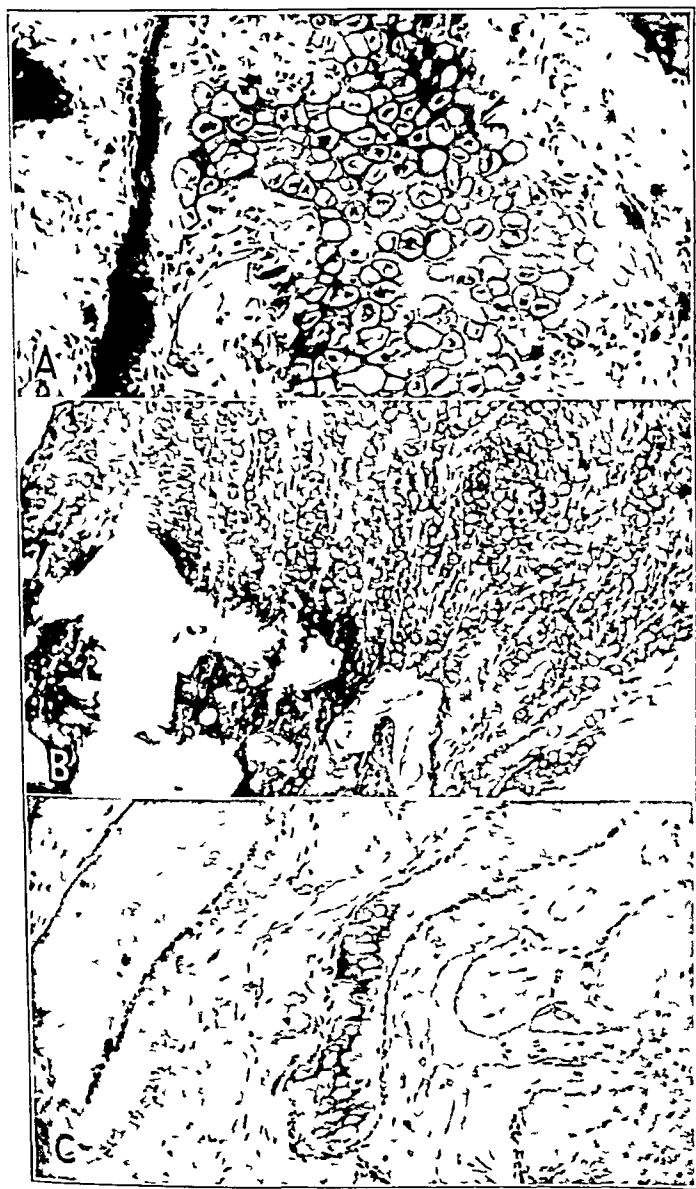


Fig 1—*A*, masses of hyaline cartilage continuous with bone trabeculae (case 2), *B*, masses of fibrocartilage extending into bone trabeculae (case 4), *C*, bone tissue with cartilaginous residue (case 7), $\times 99$

cartilaginous tissue along the margin of the bone merged directly with the trabeculae (fig 1 B)

CASE 5—While playing football in November 1931, a youth aged 18 was struck on the posterior surface of his right thigh. Swelling and slight induration of the tissues developed. On May 5, 1932, Dr E L Ryerson removed a mass of bone loosely attached near the center of the posterior surface of the right femur. A piece from the attachment of the bone to the femur measured 2 by 1 by 0.7 cm, the main portion was 7 by 2.7 by 0.5 cm. Another mass measured 3.8 by 1.7 by 1.3 cm, broken fragments together equaled a mass 3 by 3.5 by 1 cm.

Portions from the attachment of the bone to the femur had marginal scar tissue that extended into cartilage or fibrocartilage (fig 2 A), directly continuous with bone trabeculae. Some of these bone trabeculae had residues of hyaline cartilage. The main mass of bone was similar. Some of the trabeculae were osseous cartilage (fig 2 B), others were incompletely developed bone (fig 2 C). Loosely arranged fibrous connective tissue filled the interstices between the trabeculae.

CASE 6—The right thigh of a Negro aged 29 was struck by an automobile. A swelling anteriorly in the middle third of the thigh became hard. After three and one-half months the mass was excised by Dr H E Mock. There were many broken pieces of bone. Two of these were 6.8 by 2 by 1.5 cm and 5.5 by 1 by 1.2 cm respectively. The remainder equaled a mass 8 by 6 by 3 cm.

Many trabeculae were lamellar bone, others had irregular residues of ossifying cartilage (fig 3 B). Islets of cartilage or fibrocartilage mingled with the bone (figs 3 A and 3 C). Some of the bone trabeculae along the margins extended into masses of fibrocartilage continuous with organizing scar tissue. Vascular fibrous tissue was between the trabeculae.

CASE 7—A white man aged 24 was kicked accidentally on the front of the left thigh. A small, slightly painful swelling resulted and was treated with ultraviolet rays for ten days, when it became large. About a pint of serous guineous fluid was removed. After a few days several more ounces were removed but no fluid was recovered a week later. Roentgenograms at this time had no unusual shadows, but after three weeks a density was demonstrated in the soft tissues. A small piece removed surgically was diagnosed as osteofibrosarcoma. The patient was admitted to St Luke's Hospital in the care of Dr H E Mock five weeks after the injury. Skeletal muscle containing a Y-shaped piece of bone was removed from the front of the middle third of the left thigh. The bone was 12 cm long and 7.5 cm wide. One limb had diameters of 3.5 and 2.2 cm, the other, of 4 and 3.2 cm. A mass of bone at the bifurcation was 3 by 2 by 1.5 cm. A severed pedicle on one side of the Y-shaped piece was 7.5 by 1.5 cm. Another flat piece of bone was 7.5 cm long, 3 cm wide and 1.1 cm thick. One side was continuous with the pedicle of the Y-shaped tissue, the other with the femoral attachment. Two pieces of bone and muscle tissue were 4 by 2 by 0.8 cm and 2.2 by 1.2 by 0.5 cm respectively.

Most of the trabeculae in the portions examined were lamellar bone, a few contained small masses of cartilage (fig 1 C). The associated edematous and fat tissues had a few skeletal muscle fibers.



Fig 2 (case 5)—*A*, fibrocartilage merging with bone in the remoral attachment of the callus *B* ossifying cartilage *C* incompletely differentiated bone, $\times 99$



Fig 3 (case 6) —*A*, fibrocartilage and hyaline cartilage extending into osseous trabeculae, *B*, trabeculae of bone with residue of cartilage, *C*, cartilage merging with osseous tissue, $\times 99$

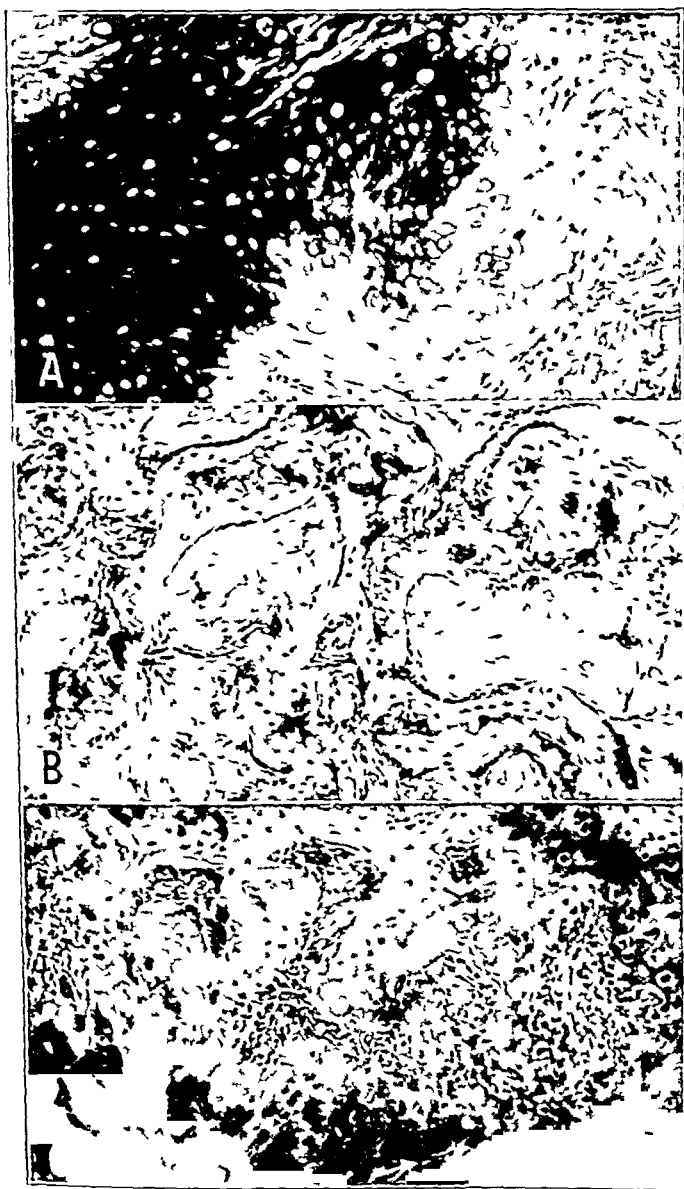


Fig 4—*A*, masses of fibrocartilage which extended into bone (case 8), *B*, trabeculae with residue of cartilage (case 9), *C*, cartilaginous tissue merging with osseous trabeculae (case 9), $\times 99$

CASE 8—The right thigh of a white youth* aged 17 was bruised during a basketball game. The muscle tissues in front became swollen and indurated. After two and one-half months an irregular mass of bone and skeletal muscle 9 by 5 by 2.5 cm was removed by Dr H B Thomas. Portions of the mass were fibrous or skeletal muscle tissue containing hard and soft bone, others had the consistency of cartilage. Six smaller pieces of bone also were removed.

Irregular masses of cartilage or fibrocartilage continuous with dense scar tissue extended into poorly differentiated bone (fig 4A). Many trabeculae contained large residues of a cartilage matrix. The portions between were edematous fibrous tissue.

CASE 9—A white man aged 49 dislocated his right shoulder. With the clinical diagnosis of myositis ossificans, bone tissue was removed by Dr W R Cubbins from the region of the shoulder sixty-seven days later. Six pieces of tissue ranging between 4 by 1.5 by 2 cm and 1 by 0.5 by 0.5 cm were submitted for histologic examination.

This tissue showed various stages of osseous growth and differentiation. There were differentiated bone trabeculae, others with residues of a cartilage matrix (fig 4B) and columns of hyaline cartilage merging into fibrocartilage (fig 4C). The cartilaginous trabeculae had traces of a fibrillar structure. Fibrocartilage constituted a large part of the tissue.

CASE 10—A Negro aged 43 had a straight transverse fracture without dislocation of the distal third of the left radius. A cast was applied for three weeks. After two and one-half months the left forearm still was swollen and stiff. A shadow about the bone in the roentgenograms suggested a sarcoma. A section of bone tissue 4.3 cm long and 2.5 cm wide, chiseled by Dr W R Cubbins from the cortex of the radius, extended into a ridge of bone 3.5 cm long, 1.5 cm wide and 1.2 cm thick. Another section of bone tissue was 9 by 0.9 by 0.5 cm, small pieces equaled a mass 3 by 3 by 1.5 cm.

The piece of tissue removed from the radius was cut into five blocks for histologic examination. A large amount of fibrous scar tissue covered the bone. Many trabeculae were lamellar bone, some had residues of a cartilage matrix. Masses of fibrocartilage along the edge were continuous with bone. The trabeculae near the fibrocartilage were not fully differentiated and had residues of fibrocartilage. The central portions of the mass had large amounts of fibrocartilage that merged directly into trabeculae of undifferentiated and lamellar bone (fig 5A). Many had residues of cartilage.

CASE 11—A white man aged 38 had symptoms of obstruction of the lower part of the bowel. On Sept 24, 1938, Dr W R Cubbins resected a carcinoma in the distal portion of the sigmoid through a suprapubic midline incision. Two pieces of mucosal tissue measuring respectively 3.5 by 3 by 2 cm and 2 by 1 by 0.7 cm were removed on October 20 from the colostomy opening. The sections contained aggregates of carcinoma cells and a small mass of bone several millimeters in maximum diameter. The slender bone trabeculae were poorly differentiated. Many had a fibrillar matrix (fig 5C) resembling fibrocartilage, some had masses of cartilage (fig 5B).



Fig 5—*A* cartilaginous tissue extending into trabeculae of bone with residue of cartilage (case 10), *B* cartilage and ossifying trabeculae (case 11), *C* ossifying trabeculae with a fibrillar matrix (case 11) $\times 99$

Cartilage and fibrocartilage occurred in varying amounts in the callus tissues examined. The amount, distribution and structure seem to depend on the stage of growth. In an old callus composed of lamellar trabeculae of bone no cartilage tissue, or only traces of it, remained. Large amounts of cartilage or fibrocartilage were observed in callus tissues of recent origin. In the reviews of traumatic ossification mentioned, the presence of cartilage suggested the possibility of endochondral bone formation. This tissue usually was considered incidental in the development of the callus or metaplastic in intramuscular connective tissue. Goto expressed the belief that the formation of cartilage depends on osteogenic cells. According to Lauche,¹² all fractures of bones were believed to heal through a cartilaginous stage of callus formation. Studies of healing fractures in human and other animal bones have demonstrated that the callus with complete immobilization contains no cartilage. This tissue develops, however, when the fractured ends grate on each other, that is, when the callus at the fracture is injured by motion. Cartilage is present regularly in the callus about fractures of ribs. These differences in the cartilage content of tissues in healing fractures suggest the possibility that cartilage develops from some component other than bone. The fate of cartilage tissue in a callus may be one of several. Usually, according to Lauche, it is transformed by endochondral ossification into lamellar bone. In his discussion of the cartilaginous tissue in parosteal callus, Lauche conceded that such tissue may develop without the stimulus due to motion.

The tissue of traumatic ossification in the early stages of growth has considerable cartilage (cases 8, 9, 10 and 11). These growths have cartilage in direct continuity with partially differentiated trabeculae of bone, as well as trabeculae with residues of a cartilage matrix. The theories proposed for the origin of parosteal callus tissues and reviewed in the introductory paragraphs of this report vary widely in view and probability. None emphasizes the fibrocartilage and cartilage components as stages in the formation of the bone. If fibrocartilage is basic in the evolution of the parosteal tissues, there should be normally in regional tissues a similar matrix which, reacting to trauma by reparative growth, develops into the ossifying lesion. Such a direct process would explain more satisfactorily the actual conditions encountered.

According to textbooks on histology,¹³ fibrocartilage occurs, among other places, in the ligamentum teres femoris and in the attachments of certain tendons to bones. Because many of the parosteal callus tissues

12 Lauche, A., in Henke, F., and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1937, vol. 6, pt 3.

13 Maximow, A. A., and Bloom, W. *A Textbook of Histology*, ed. 2, Philadelphia, W. B. Saunders Company, 1935, p. 116.

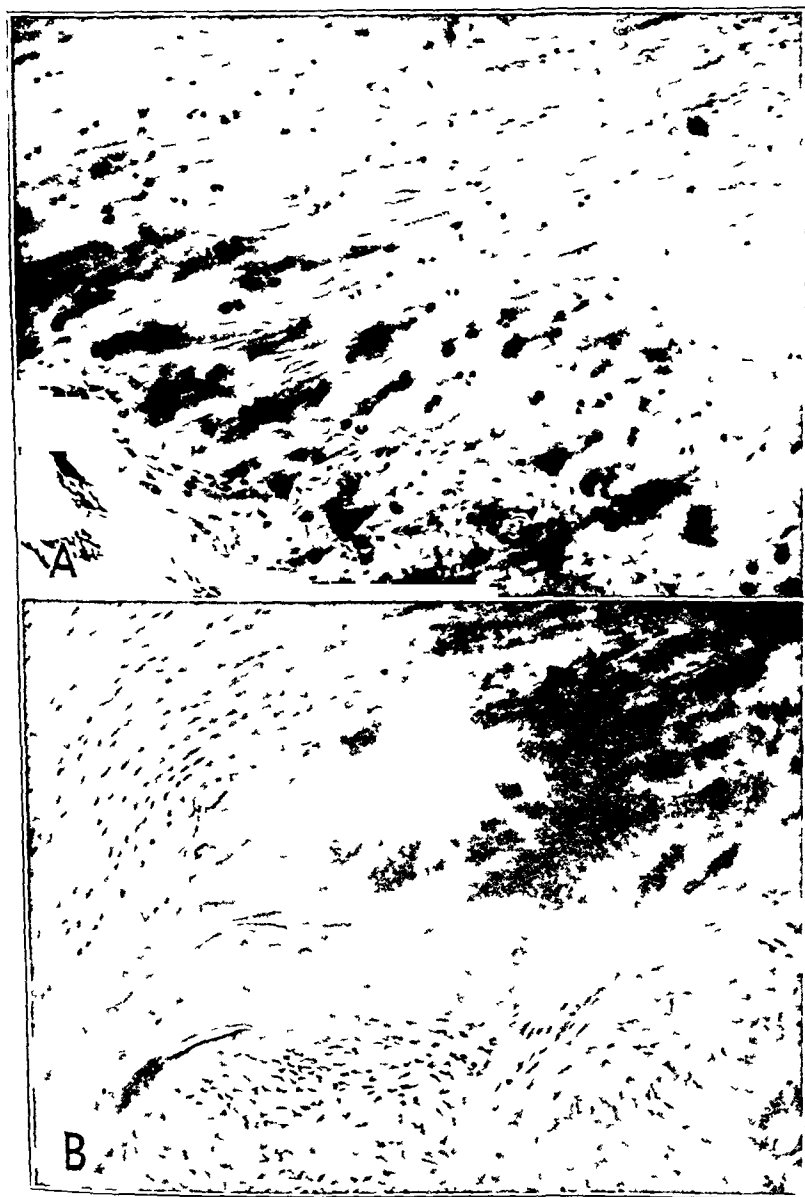


Fig 6—*A*, latent fibrocartilaginous tissue in the insertions of tendons from adults. *B* latent fibrocartilaginous tissue in the insertions of tendons from adults, $\times 111$

occur in tendon attachments, a search was made therein for fibrocartilage. Tendon insertions with a thin plate of bone of the brachialis anticus, biceps brachialis, semitendinosus, semimembranosus, quadriceps femoris and gastrocnemius muscles were removed from 25 cadavers, male and female, the patients having died from various causes at ages between 0 (full term delivery) and 76 years. The tendons were cut 1 to 2 cm from their insertions. The tissues of 69 tendons were fixed in Zenker's solution, decalcified and embedded in pyroxylin (celloidin), and the sections were stained with hematoxylin and eosin (some with phosphotungstic acid and hematoxylin). The tendons of infants had compact parallel collagenous fibers. Between the fibers were numerous stellate fibroblasts with oval vesicular nuclei. At a point 1 to 2 mm from the attachment to the bone, compressed cartilage cells lay between the tendon fibers. Near the bone the tissue was dense fibrocartilage with a considerable hyaline matrix. In the adult tendons was a narrow layer of fibrocartilage at the junction with the bone (fig 6). The thickness of this layer varied in different cadavers and in different portions of a single insertion. The width ranged between 1 mm and a few microns. Fibrocartilage was present in all. The places examined, of course, did not include all portions of the skeleton or all tendinous insertions. The study demonstrated that fibrocartilage is distributed as a normal tissue constituent in places where traumatic ossification occurs.

COMMENT

The abundance of fibrocartilage or cartilage in callus tissue during the early stages of traumatic ossification and the small amount or the absence of these components in fully organized tissue in the late stage suggest that the cartilage matrix is a transition into bone rather than that cartilage develops from the bone. Stages of development from cellular fibrocartilage or hyaline cartilage into trabeculae of poorly differentiated bone and trabeculae of lamellar bone with residues of a cartilage matrix occur regularly in incompletely differentiated callus tissue. Such arrangements imply that the bone trabeculae develop through a process of endochondral ossification. The fibrocartilage which is a normal constituent of many tendon insertions is probably the matrix from which traumatic ossification develops. It is reasonable that a reactive or reparative growth of these tissues provoked by an injury results in the disturbance known as traumatic ossification or myositis ossificans. Evidence that these cartilaginous stages occur in the ossification of tissues near but perhaps not directly continuous with bone is found in case 11.

Endochondral genesis is accepted as a natural process in the development of bone. Accordingly, recourse to the theory of metaplasia

connective tissue with its implications, as an explanation of bone formation is unnecessary when fibrocartilage tissues with potentials of bone production have proliferated

SUMMARY

In the early stages the lesion of traumatic ossification contains large amounts of fibrocartilage or hyaline cartilage continuous into bone with varying degrees of differentiation. Some portions seem to be ossifying cartilage, others have lamellar trabeculae containing residues of cartilage. In the late stages of the lesion there are a high content of lamellar bone and only small traces of cartilage. These conditions imply the origin of bone in a cartilage matrix, that is, endochondral bone formation.

Fibrocartilage is a normal constituent of the insertions of many tendons in which traumatic ossification occurs. A reactive or reparative growth of these tissues initiated by trauma provides a simple explanation for the lesion of traumatic ossification.

REVIEW OF UROLOGIC SURGERY

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KIDNEY

Surgical Technique—Fagerstrom¹ stated that nephroureterectomy is an operation that should be reserved for certain uncommon types of pathologic conditions. Its indication, while at times precise, can be determined only by a thorough preliminary examination of the patient including the making of proper ureterograms.

The indication for nephroureterectomy in cases of papillary tumor of the renal pelvis is today unquestioned. In other types of pathologic lesions the indication hinges mainly on the size and hydrodynamics of the ureter. When grossly infected kidneys are removed, it is unwise to leave behind a large, nondraining ureteral pouch.

The difficulties of total ureterectomy are not prohibitive, and when combined with nephrectomy the additional time involved is usually minimal and sequential. The patient presenting average surgical risk withstands the combined procedure with no greater shock than that attending a

¹ Fagerstrom, D. P. Ureterectomy. Its Indication as in Papillary Nephrectomy, *J Urol* **41** 137-150 (Feb) 1939

nephrectomy. Secondary ureterectomy is usually performed after months of ill health have debilitated the patient and the technical problems encountered may be difficult in the extreme. When employed with proper selection, total primary ureterectomy will often circumvent many of the pitfalls of misguided conservative surgical treatment.

Nephrostomy—Nephrostomy is a conservative operation for temporary or permanent drainage of the kidney; it will preserve renal function or provide an avenue of escape for retained products of infection in the presence of ureteral occlusion. Obstruction of the kidney and the factors affecting its recoverability have been considered.

Graves and Buddington² discussed the following indications for nephrostomy as encountered in their series of cases: drainage of the kidney following removal of stones through its cortex, drainage of the kidney during healing of the lines of suture following plastic operations on the renal pelvis or upper portion of the ureter, ureteral occlusion by malignant disease, acute ureteral occlusion by edema following electrocoagulation or irradiation in cases of tumor of the urinary bladder, bilateral nephrolithiasis with marked impairment of the total renal function, as the first step in a two stage nephrectomy, bilateral hydro-nephrosis, usually congenital in origin, and often associated with atony of the ureter above and below the point of stenosis, with marked impairment of the total renal values, obstruction of the ureter by impassable inflammatory stricture, in association with ureterointestinal anastomosis, as a life-saving measure in cases of profound toxemia arising from severe pyelitis of pregnancy in which milder measures have failed.

Anomalies—Braasch and Hammer³ stated that the clinical recognition of renal fusion has become more frequent in recent years as a result of the routine use of excretory urography. Clinical recognition by this method was possible in 95.5 per cent of 102 cases reviewed.

The position of the renal pelvis in cases of bilateral fusion is variable, but the following features are of interest: (1) the low situation of one or both renal pelvis in relation to the vertebrae—more than 60 per cent being below the third lumbar vertebra—and (2) the closer proximity of the right pelvis to the vertebral margin when the right and the left pelvis are compared. Although in the presence of renal fusion the two pelvis usually are situated closer together than normally, the distance separating them is not uniform, and it may be so great that the presence of fusion would seem impossible.

² Graves, R. C., and Buddington, W. T. Nephrostomy. Indications and Technique, *J. Urol.* **41**: 265-281 (March) 1939.

³ Braasch, W. F. and Hammer, H. J. Renal Fusion. Urographic Data and Their Clinical Significance, *Tr. Am. A. Genito-Urin. Surgeons* **31**: 321-332, 1938.

In differential diagnosis, which may be difficult, the possibility of the presence of the following conditions should be eliminated (1) bilateral renal fusion and incomplete renal rotation with ectopia and (2) unilateral renal fusion and crossed renal dystopia without fusion

Evidence of dilatation of either the calices or the pelves, or both, is associated in many cases with renal fusion. This condition usually indicates the presence of stasis. Pyelectasis and caliectasis are sometimes observed in patients who have never had pain. Lumbar pain is sometimes observed in patients who do not have evidence of pyelectasis or caliectasis. Fused kidneys removed at necropsy may show gross evidence of a minor degree of pyelectasis without apparent ureteral obstruction. In some cases, this may be a residual deformity caused by previous obstruction. The existence of renal stasis can best be demonstrated by the use of delayed retrograde urography, and renal stasis will be found present to a variable degree in many cases of renal fusion. It may be a variable factor in indicating the cause of obscure lumbar or abdominal pain.

Soloway⁴ stated that bilateral metanephric agenesis is a rare anomaly, and is a condition incompatible with extrauterine life. The infant is frequently alive at birth, but death occurs in a few hours. This condition is usually associated with other equally serious defects of development. In a thorough review of the literature, Amolsch reported 119 cases, including 4 of his own. Twelve cases of renal anomalies observed at postmortem examination were reported. Two more cases of bilateral renal agenesis were reported by Soloway, making the total number of cases reported 121. Bilateral renal agenesis is observed in about 1 of 6,000 necropsies. Soloway also recorded 10 cases of congenital solitary kidney. Of these, the kidney, ureter and ureteral orifice were absent in 8, rudimentary ureters were present in 2, associated genital anomalies were observed in 3, and the adrenal gland was absent in 2 and not recorded in 8. Bilateral renal agenesis is usually found at necropsy, but unilateral renal agenesis is diagnosed more frequently, and proper treatment instituted much earlier than previously, as the result of improved diagnostic methods and more general employment of intravenous urography.

Shoemaker and Braasch⁵ stated that the ratio of cases of fused kidneys as observed at necropsy at the Mayo Clinic was 1:385. All age groups were well represented in this series of cases. In 24 cases the ureters, pelves and calices were normal except for their position in relation to

4 Soloway, H. M. Bilateral and Unilateral Renal Agenesis. *Ann. Surg.* 109:267-273 (Feb) 1939.

5 Shoemaker, R., and Braasch, W. F. Fused Kidneys. A Study of the Gross Pathologic Changes in Thirty-Five Cases. *J. Urol.* 41:17 (1939).

the renal parenchyma. In 11 cases there was some degree of dilatation of the ureters, pelvis or calices. In 5 of these 11 cases the dilatation was limited to the calices and pelvis and could be considered the result of the anomaly. The cause of the obstruction in the upper third of the ureter could not be definitely ascertained in a sixth case. There were 8 cases of hypertrophy of the prostate gland and 1 of stricture of the urethra in the total of 35 cases. In 6 of these cases there also was some dilatation of the upper part of the urinary tract, and in 4 of the 6 cases the dilatation was probably secondary to the obstructing lesion in the lower part of the urinary tract. Dilatation was secondary to a vesicocolonic fistula in another case. In 2 of the 35 cases the possibility of fused kidney was suggested by pyelographic examination, but in another case the diagnosis could not be made by this means. Sections were examined microscopically in 21 cases. Fourteen specimens were not available for section. Ten of these specimens appeared grossly normal. Coexistent congenital anomalies were present in 11 cases.

Calculi—Howze⁶ reported 4 cases of large and multiple renal calculi in children. Chronic pyuria is the predominating symptom of large calculi in children. The occurrence of renal calculi in one kidney with coexisting pathologic lesions of the second kidney makes conservative surgical treatment imperative in many cases. The possibility of the dissolution of cystine calculi by medical means demands a more careful study of the urine for cystine crystals in all cases of children having urinary stones. Surgical treatment of the urinary tract is well tolerated by children, and gratifying results frequently can be obtained in cases of badly damaged kidneys.

Hellstrom⁷ said that most urinary infections probably can contribute in some way or another to the formation and development of concrements but that infection by staphylococci stands alone in this respect, since it is the most common cause of so-called infection stones and since it produces a uniform type of concrement.

Hellstrom's conclusions were drawn from 100 cases of what he called "primary staphylococcus stones of the kidney and ureter." All calculi with any etiologic factor other than a staphylococcic infection were excluded.

Analysis of 750 cases of renal and ureteral calculi at the Maria Hospital, Stockholm, showed oxalate stones in 63 per cent of the cases, infection stones in 22 per cent and uric acid and phosphate (aseptic) stones of uncertain composition and cystine stones in 5 per

⁶ Howze C P. Large and Multiple Renal Calculi in Children, *Tr Am A Genito-Urin Surgeons* **31** 1-20 1938.

⁷ Hellstrom J. The Significance of Staphylococci in the Development and Treatment of Renal and Ureteral Stones. *Brit J Urol* **10** 348-372 (Dec) 1938.

cent, each. Seventy-five per cent of the "infection stones" were caused by staphylococci, of these, 57 occurred in men and 43 in women. Ninety-six per cent of the patients were between the ages of 20 and 50. Thirty per cent of the stones were bilateral, a higher percentage than is generally found for aseptic stones because staphylococcuria is often bilateral. Likewise, multiplicity is more frequent in the infectious than in the aseptic type.

Of the 100 patients observed, 74 had renal stones and 45 had ureteral stones. Analysis of the stones in this series showed all of them to be composed of amorphous phosphates, triple phosphates and calcium carbonate, in varying proportions.

The organic substance of the stones was largely composed of staphylococci, and after decalcification and staining, these organisms were seen lying in concentric layers in an amorphous fibrillar substance.

Patients having these stones generally give a history of a long-standing, low grade urinary infection with recurrent attacks of cystitis or pyelitis. There is often a whitish, sandy admixture in the urine near the completion of micturition, and there is chronic staphylococcuria. Because these organisms split urea, the urine rapidly becomes alkaline if it stands. Despite the fact that staphylococci appear in masses in the sediment, they grow poorly in the common nutrient culture mediums, so that staining the fresh specimen is of great importance.

Hellstrom said that every patient having staphylococcuria should have a careful roentgenologic examination, including a ureteropyelogram. Cystoscopy often shows few cystitic changes, and the marked ulceration and incrustation which Rovsing stated were characteristic of urinary infections with urea-splitting organisms were not observed in Hellstrom's cases. Likewise, there was little parenchymal suppuration in the kidneys. The chief condition was pyelitis and ureteritis with round cell infiltration in the submucosa, most pronounced in the niches of the calices. Hellstrom said that formation of stone often begins there.

Treatment of the staphylococcic infection is not effective unless the stones have been removed or are passed at micturition.

General measures consist of acidification of the urine by means of the acid ash diet and calcium or ammonium chloride. Although Hellstrom found no evidence in his large series of cases of urinary stones that avitaminosis was an etiologic factor, he prescribed administration of vitamin A postoperatively.

Vaccines and bacteriophage are of little value. Sulfanilamide can be used, but the best preparation is neoarsphenamine in doses of 0.15 to 0.3 Gm. every three or four days. Administration of acetarol by mouth is of value. Lavage of the renal pelvis with a mixture of

tion of boric acid and potassium permanganate (1:4000) has been useful. Hellstrom said that this mixture is the best of the preparations commonly used for this purpose.

Conservative treatment consisting of expectant therapy, ureteral catheterization and pelvic irrigation was employed for 20 of his patients, resulting in cures for 18.

Of the 80 patients operated on, 31 had ureterolithotomy, 28 pyelolithotomy, 25 nephrectomy, 21 nephrolithotomy, 2 renal resection, 1 ureterostomy, 3 decapsulation and nephrostomy and 2 suprapubic cystostomy, plus snipping of the ureteral orifice. There was 1 death, a mortality rate of 1.25 per cent.

The late results were as follows:

	No. of Cases
No stones, sterile urine	26
No stones, bacilli	7
No stones, staphylococci	3
Stones still present, no new ones	8
Recurrence on the side of operation probably arising from remaining stones	5
Recurrence on the side of operation from new formation of stones	11
Recurrence on the other side by new formation	6
Recurrence on both sides by new formation	8
Results uncertain	5

Recurrences probably arising from remaining stones were observed in 5 cases, and genuine recurrences arising from new formation of stones were observed in not less than 25 cases. The genuine recurrences appeared on both sides in 8 cases, on the side of operation only in 11 cases and on the opposite side only in 6 cases. Thus, altogether, 19 patients had genuine recurrences on the side of operation, 6 of these patients had undergone pyelolithotomy, 5 nephrolithotomy and 8 ureterolithotomy. Nearly half the recurrences appeared within the first year after operation and 2 within only one month after operation. If the patients with stone bilaterally are included, recurrences were observed on the side opposite that of operation in 14 patients, 3 of whom had undergone pyelolithotomy, 2 nephrolithotomy, 4 ureterolithotomy, 1 suprapubic cystostomy and papilloolithotomy and 4 nephrectomy. Generally, the recurrences took a longer time to appear on the intact side than on the side of operation.

The most important cause of recurrence is persistent or recurrent staphylococcal infection. The fact that most recurrences occurred after ureterolithotomy is evidence against the importance of operative trauma for in the presence of aseptic stones ureterolithotomy is the operation least likely to be followed by recurrence.

Of the patients having recurrent stones, 12 later underwent one or more operations for the condition, and in 15 instances spontaneous passage occurred. This resulted in 18 of the patients with recurrent stones becoming free from stones, and of these, 8 have also become free from bacteria. Of all the patients operated on—primarily or for recurrence—only 34 (42.5 per cent) have been freed from calculi and bacteria. The prognosis in operations for staphylococcic stones is thus rather poor so far as complete cure is concerned.

Measures to improve these results consist in taking roentgenograms at the time of operation, lavage of the renal pelvis after it has been opened, drainage of the stoma created by nephrostomy, correction of obstruction by nephropexy, ureterolysis, plastic surgical treatment of the renal pelvis or renal resection, and initiation of measures to control the infection after operation. Nephrectomy may be the most conservative operation at times. In Hellstrom's series, recurrences were present in the remaining kidney after nephrectomy in only 1 instance (4 per cent), while after conservative measures had been instituted recurrences were present on this side in 20 per cent of cases.

Smith⁸ stated that renal infection is not a factor of major importance in the formation of the majority of primary renal calculi. In the formation of recurrent stones, except those caused by hyperparathyroidism and cystinuria, infection is of the greatest importance. In such cases *Bacillus proteus* is the organism most commonly observed. The urologist's duty is not fulfilled by removal of the stone; he must then employ every known measure to eradicate the renal infection. In order to do this successfully, he must vary his surgical procedure according to the circumstances in the case. This may mean performance of nephrectomy, partial nephrectomy, nephrostomy or pyelotomy. In no instance of renal stone should the outcome be regarded as satisfactory until the urine of the patient has become sterile.

Jáki⁹ discussed the formation of renal calculi in cases in which vitamin A is lacking. He stated that avitaminosis in rats causes stones in a large percentage of cases. The urine of these animals is alkaline and infected, and the stones are usually phosphatic. Avitaminosis rarely occurs in man, because vitamin A is found frequently in the common foodstuffs. On the other hand, in fully 90 per cent of cases renal stones are unilateral. Jáki offered these two facts to refute the statement that stones in man are frequently associated with lack of vitamin A. He further stated that with the exception of Huggins, the investigator had been able to prove that avitaminosis or hypovitaminosis

⁸ Smith, G. G. Renal Infection and Nephrolithiasis, *Surg. Gynecol. Obstet.* 68: 527-533 (Feb. 15) 1939.

⁹ Jáki, J. Das Vitamin A und die Harnsteinbildung, *Ztschr. f. klin. Med.* 75: 750-756 (Nov.) 1938.

was the cause of formation of stone in his patients. In the advanced stage there is a decrease in the concentration of vitamin A in the blood and tissues. Stones are more common in young persons, who have larger amounts of vitamin A than others. Jaki concluded that the administration of vitamin A may aid in the prevention of recurrence of stones but that it should be used only as an adjunct to other means of prevention of the formation or recurrence of stone.

Harbitz¹⁰ stated that after appendectomy pathologic constituents in the urine are not infrequently found, and that in about 1 per cent of the cases hematuria is macroscopically visible. Hematuria usually appears in the course of the first eight days after operation, and is encountered especially in children—in Harbitz' experience, chiefly in little girls. The nature of the hematuria has not been ascertained, but it must be supposed to be caused by hemorrhagic nephritis. Often *Bacillus coli* is found in the urine at the time of hemorrhage. In cultural experiments, however, it has not been possible to obtain a growth of bacilli which might be the cause of the renal disturbance and the hemorrhage.

The hematuria is in general not attended by important symptoms, but all degrees of hematuria have been found, up to serious acute hemorrhagic nephritis, which may end in complete anuria.

The prognosis seems to be good in all cases. Even patients having anuria progressed to good health and the illness seemed to have been cured.

In a few cases the postoperative hematuria may be due to formation of concretions in the urinary tract soon after appendectomy. In other cases it is seen that urinary concretions are formed a long time after the appearance of postoperative hematuria, and these stones cause attacks of pain and renewed hematuria. Such formation of calculi was, in Harbitz' material, seen in 3 children. This is unusual, since formation of concretions in childhood is otherwise of rare occurrence in Norway.

Tumors—Cabot and Middleton¹¹ stated that renal adenomas occur most frequently in the years of greatest incidence of degenerative vascular disease. There is no conclusive evidence to contest the repeated assertion that adenomas are usually formed as a result of occlusion and dilatation of renal tubules.

The cystic spaces commonly seen in papillary adenomas probably represent in most cases, the stage of development preceding the forma-

10 Harbitz H F. Haematuria and Renal Calculus as Complication After Appendectomy. *Acta chir Scandinav* 81:405-424 (Jan 13) 1939.

11 Cabot H and Middleton A W. The Relation of So-Called Adenoma of the Kidney to Carcinoma of the Kidney. *Tr Am A Genito-Urin Surgeons* 31:91-105 1938.

tion of the multiple papillary projections that compose this tumor. However, the presence of calcium and other evidences of chronicity in some instances suggests that cysts may also occur as a result of degeneration of an adenoma. One microscopic section suggested that adenomas may occur in association with polycystic disease.

The renal adenoma is not a transitional stage between tissue of benign character and tumors of known malignancy, as is commonly stated, but is itself a malignant growth.

Bugbee¹² stated that a malignant condition of the urinary tract, whether located in the kidney, bladder or prostate gland, can be cured only by complete removal while the lesion is still localized. This procedure can be effected only on the basis of an early diagnosis, which may be difficult because of the late appearance of physical signs and symptoms suggesting the presence of a malignant growth.

Nephrectomy, carried out under satisfactory exposure and with as little traumatism as possible, will result in a certain number of cures.

Tumors of the bladder, although easily diagnosed, are often allowed to become extensive before being discovered. Fulguration and transurethral resection produce excellent results in cases of low grade papillomas and in certain instances of papillary carcinoma, whereas infiltrating carcinoma is often radioresistant and the only surgical treatment applicable may be total cystectomy following deviation of the urinary stream.

Cancer of the prostate gland is essentially a fatal disease. Rarely is complete removal of the lesion possible. As a rule, by the time the diagnosis has been made the disease has extended beyond the capsule, and the surgeon's efforts may best be expended in restoring urinary function, a procedure which may be accomplished with a minimum of risk to the patient by means of transurethral resection. It should be borne in mind that most cancers of the prostate are of slow growth.

The watchword should be "early diagnosis," with constant emphasis on the necessity of ascertaining the origin of erythrocytes found in the urine, for only through such means will the surgeon be able, in the light of present knowledge, to substitute methods of cure for palliative treatment in the management of malignant genitourinary tumors.

Barney and Churchill¹³ stated that adenocarcinoma of the kidney (hypernephroma) may on occasion be treated by removal of the primary growth and that this tumor apparently has but a single metastasis. He reported the case of a patient in whom roentgenologic evidence of a metastatic nodule in the lung was the first sign of disease. Nephrectomy

12 Bugbee, H. G. *Surgery of Genito-Urinary Malignant Tumor*. J. Urol. **112** 298-301 (Jan. 28) 1939.

13 Barney, J. D., and Churchill, E. D. *Adenocarcinoma of the Kidney with Metastasis to the Lung, Cured by Nephrectomy and Lobectomy*. J. Urol. **31** 71-79, 1938.

was performed five months later and fifteen months after nephrectomy the pulmonary metastasis was excised by subtotal lobectomy. The patient was alive five years later and in good health, without evidence of disease. Barney and Churchill stated that metastases to the lung occur not infrequently as the result of adenocarcinoma of the kidney. There is clinical and roentgenologic evidence that these metastases may occasionally undergo spontaneous regression.

Hemorrhagic Cysts—Scholl¹⁴ reported a case of hemorrhagic cyst of the kidney in a man 58 years of age, who had had a swelling of the abdomen for three years. A tumor was found in the region of the left kidney, the tumor spread from the left costal margin to the lower part of the right flank, almost completely filling the left side of the abdomen and extending into the right side. The patient had undergone prostatectomy six years previously, at which time he had pain in the region of the left kidney. Roentgenograms of the abdomen disclosed a large, rounded tumor of soft tissue, filling the left side and extending across the midline into the right side. Peritoneoscopy disclosed that the left lobe of the liver was pushed to the right and that the stomach was displaced upward by a large tumor, which occupied three fourths of the abdominal cavity. Cystoscopic and pyelographic examination showed moderate dilatation of the pelvis, in the upper region of the tumor. It was thought that the kidney was separate from, and not involved in, the structure of the tumor.

The tumor was explored surgically through a straight left rectus incision, with the patient under gas anesthesia. The colon was pulled toward the midline, and an opening was made in the mesocolon of the descending colon and the upper portion of the sigmoid flexure. The left kidney was large, and on both poles and projecting from its under surface were several large cystic dilatations, which extended from the diaphragm to the pelvis and across to the lower right abdominal quadrant. The entire cystic mass was gently dissected out, most of it by blunt, but some by sharp, dissection. Because of firm adhesions, it was impossible to remove the mass intact. When it was torn, a large amount of old, chocolate-colored clots and black fluid escaped from the cystic mass. The patient readily recovered after the operation.

The specimen removed consisted of the enlarged kidney and an extremely dilated sac. The capsule of the kidney was continuous over the wall of the cyst, the wall varying from 3 to 6 mm in thickness. There was no evidence of involvement of renal parenchyma in the wall of the cyst, such as is usually seen in cases of hemorrhagic cyst. The inner layer of the wall was composed of old hemorrhagic masses of

¹⁴ Scholl A J Hemorrhagic Cysts of the Kidney J Urol 41 103-110 (Feb) 1939

organized clots and fibrin. Some of the clots were extremely adherent to the wall of the cyst and could be removed only by tearing. The cyst, which on external examination appeared to be multilobular, was solitary and was filled with organized and partly organized blood clots, together with a large amount of thin black fluid. Some of the clotted masses were apparently old, since they contained shreds of fibrin and were hard and difficult to tear apart. At the base of the cyst there was a tumor about 8 cm. in diameter, which had spread through the renal capsule to infiltrate the tissues around the ureter and renal vessels. Histologically, this tumor was a rapidly growing papillary adenocarcinoma of the clear cell type.

Tuberculosis—Wildbolz and Walthard¹⁵ stated that it is generally admitted that the early foci of renal tuberculosis are found in the papillae. Tuberculous changes in the renal cortex seem to be either secondary or the result of miliary tuberculosis. Wildbolz and Walthard speculated on the possibility that these changes in the cortex may in some cases be the primary lesion.

Medlar's studies led him to believe that this may often be the case. The kidneys he examined were those taken from patients who had died of tuberculosis, but whose urinary tracts had not been examined before death, consequently, Medlar's results are not above criticism.

Wildbolz and Walthard described a case which definitely proved that chronic renal tuberculosis may start in the cortex. Acid-fast bacilli were found in the urine from the right kidney of a girl of 19 years. Long search revealed nine small foci in the renal cortex, and none elsewhere.

Clairmont and Schaffhauser¹⁶ stated that in their experience with a large number of cases of congenital tuberculosis they have found that the average urologist has not had sufficient training or experience to give them (the authors) the necessary information regarding the diagnosis and therapeutic progress. They further stated that even the slightest abnormal observation as to the condition of the urine should be investigated until the reason for its appearance is clear. If tubercle bacilli are found in the urine, a complete urologic examination must be made to find the focus of tuberculosis. A thorough investigation often leads to the correct diagnosis and proper treatment of the condition. The increasing interest of physicians in sanatoriums in this problem suggests that many questions which are now unanswered may be solved in the future.

15 Wildbolz, H., and Walthard, B. Die primär corticale, nicht vererbte chronische Nierentuberkulose, *Ztschr. f. urol. Chir. u. Gynäk.* **45** 1-15 1939.

16 Clairmont, P., and Schaffhauser, F. Die Nierentuberkulose, *Centr. f. Chir.* **65** 1115-1135 (May 7) 1938.

Clairmont and Schaffhauser in their clinic in Zurich Switzerland have, for many years laid great stress on the value of early diagnosis of renal tuberculosis in the teaching of students and doctors of medicine. The average physician shows a tendency to treat chronic cystitis too long without making a proper diagnosis. Clairmont and Schaffhauser distinguished between acute or subacute military and the chronic forms of renal tuberculosis. There are three types of chronic renal tuberculosis as defined by Wildbolz—the caseocavernous the nodular and the fibrous. In 11 cases of early tuberculosis the authors found the focus in or around the renal papillae. Papillary tuberculosis described by early authors is the typical initial form of chronic caseous tuberculosis. Clairmont and Schaffhauser concluded that stenosis is significant when it occurs at the ureteropelvic juncture as a result of tuberculous ulcers with only a papillary focus. Conditions of this type lead early to severe infection of the pelvis of the kidney. Patients having primary tuberculosis of the pelvis of the kidney without foci of tuberculosis in the parenchyma should be observed with care. In 2 of the authors' cases a small primary focus was observed in a renal pyramid only after a thorough anatomic examination of the kidney. Infections in the papillae may remain isolated, or originally open foci may become excluded from the pelvis resulting in clinical healing after pyuria and tubercle bacilli in the urine have disappeared. The authors have observed 3 such instances. Conditions of this type may mistakenly be considered as tuberculous bacilluria or as spontaneous healing of renal tuberculosis. Control over a long period shows that these foci as a rule recur and result in progressive urogenital tuberculosis.

Autonephrectomy may result from extensive fibrous healing and formation of scar tissue. Numerous observations have shown that renal lesions of this kind may easily initiate general tuberculosis. It is urgently advised that such kidneys be removed even though the patient exhibits no symptoms. Spontaneous recovery of patients having caseous tuberculosis with complete control, has been described only twice in the literature—once by Castaigne and once by Wildbolz. Medlar's studies do not necessarily prove that healing of this type of chronic tuberculosis can occur. His work was done on kidneys involved by a military form of tuberculosis and not by early caseocavernous infections which were discussed by Clairmont and Schaffhauser. It is possible that tuberculous nephritis a noncaseous rarely occurring form of renal tuberculosis, may eventually heal. A differential diagnosis of tuberculous nephritis and early caseous tuberculosis may be impossible to make for many years. Wildbolz has seen 20 cases of this type in more than 1300 observations and only 4 of the patients concerned showed clinical recovery which was controlled over a period of many years.

The question of tuberculous bacilluria has not been definitely settled. Clamont and Schaffhausen expressed the belief that it does not exist. The finding of tubercle bacilli in urine which has been taken directly from the kidney under proper precautions must be controlled over a period of years. Only long-continued observations may prevent errors. The authors observed a patient more than five years, the patient seemed to show spontaneous recovery, but bilateral caseous renal tuberculosis later developed. Nephrectomy is indicated only when the other kidney is healthy and when the diseased kidney exhibits marked pyuria and decreasing function. In considering the symptomatology of renal tuberculosis, Clamont and Schaffhausen emphasized so-called amictobic pyuria, which has nothing to do with tuberculosis. Statistics show that most patients having unilateral renal tuberculosis who are treated conservatively die within the first five or six years. In contrast to this are the favorable results of nephrectomy, which constitute satisfactory cures in 80 per cent of the early cases and in 50 to 60 per cent of the late cases. Early diagnosis is desirable, and early nephrectomy is the treatment of choice in cases of unilateral renal tuberculosis.

Hydronephrosis—Jewett¹⁷ stated that accessory renal vessels at the lower pole of the kidney are frequently associated with obstruction in the region of the ureteropelvic junction. In some of these cases the underlying cause is stricture, which is probably a primary pathologic entity.

In certain cases of hydronephrosis, accessory renal vessels are the chief cause of the obstruction, which is precipitated, usually in early adult life, by the effect of one or more subsidiary factors, of which the mechanism of renal growth is possibly one of the most important. Surgical intervention designed to eliminate obstructive contact is indicated. Success depends largely on the severity of infection and the extent of cortical destruction.

Odén¹⁸ reported a case of ectopic kidney. The patient, a man, had been operated on more than forty years previously because of repeated abdominal pains and a palpable cystic swelling in the lower part of the abdomen, congenital double urinary bladder being regarded as the condition responsible. At this operation a communication had been established between the two "urinary bladders." After freedom from symptoms for forty years, the patient had had pains in the left part of the abdomen. These pains had extended partly upward toward the region of the kidney and partly downward, and were associated

17 Jewett, H. J. Accessory Renal Vessels. Their Influence in Certain Cases of Hydronephrosis, *Surg., Gynec. & Obst.* 68:666-676 (March) 1939.

18 Odén, O. Ein Fall von Ectopia renis mit Hydronephrose und fortgeschrittener Degeneration, *Acta chir. Scandinav.* 81:425-438 (Jan. 13) 1939.

with frequency of micturition and occasional hematuria. On examination and surgical exploration of the left renal pelvis, a floating kidney was observed in the small pelvis, with hydronephrosis. Since the patient was having pain, the kidney was removed. On microscopic examination, the wall of the renal pelvis proved to be the seat of cancer. The parenchyma of the kidney was completely atrophic. From the communication between the hydronephrotic sac and the bladder that had been established by the operation forty years earlier, there still remained an exceedingly narrow canal. The recent symptoms which brought the patient to the physician had in all probability been caused by the subsequently detected cancer.

Notwithstanding the many brilliant results obtained with plastic procedures for the repair of hydronephrosis, the opposition to them has not subsided. Wildbolz,¹⁹ therefore, published the results obtained in the treatment of a series of patients operated on by Quinby and reexamined ten or more years after operation. Six patients had excellent function of the repaired kidney and marked improvement in the shape of the renal pelvis ten to twenty years after operation. In only 1 case had the treatment failed, the patient was found to have continuation of the hydronephrosis, with further decrease in renal function.

Parenchymal Infection—Jeck²⁰ stated that large solitary abscess of the renal parenchyma is not often seen and that it is less often recognized preoperatively. He reported 2 cases of solitary renal abscess.

In most of the reported cases in which cultures were made of the pus evacuated from the cavity of the abscess, *Staphylococcus aureus* was obtained in pure culture. Many of the patients reported on gave a history of a preexisting lesion, such as a boil or other type of staphylococcal infection of the skin.

A history of boils, carbuncles, paronychia, acute osteomyelitis, infected teeth, tonsils or similar foci of infection is of the utmost importance in establishing a diagnosis when other signs point to the kidney. In all types of such infections the physician usually observes chills to be followed by the "spiking" type of increased temperature, pain in the loin on the affected side, a moderately high leukocyte count, a low erythrocyte count with a low percentage of hemoglobin and, finally, rather marked loss in weight.

The urinary findings are often not pertinent, and are therefore frequently misleading. The urine may contain a few leukocytes or staphylococci or both, but at times does not contain either. In many

19 Wildbolz, E. Enderfolge organerhaltender Operationen bei Hydronephrose, *Ztschr f urol Chir u Gynäk* 45 31-39 1939

20 Jeck, H S. Large Solitary Abscess of the Kidney. *Tr Am A Genito-Urin Surgeons* 31 21-28, 1938

instances, functional tests of the kidney show little or no difference in the functioning capacity of the two kidneys

The treatment of large solitary abscess of the kidney is incision and drainage. On exposure of the kidney in the presence of suspected abscess, if the abscess is not at once apparent, decapsulation of the kidneys should be performed, for a solitary abscess or multiple abscesses may not be discovered until the true capsule of the kidney is removed.

The 66 cases of renal carbuncle reviewed by Graves and Parkins, together with the 36 cases reviewed by Spence and Johnston,²¹ make a total of 102 cases reported to date.

In the 36 cases reported by Spence and Johnston, there were 20 males and 16 females. The average age was 32, the youngest patient being 9 and the oldest 65. The right side was involved in 19 instances, the left in 16, 1 patient had bilateral involvement. All but 1 patient had pain on the involved side, 36 per cent had chills, and 60 per cent had fever. Unexplained weakness, malaise, loss of weight and strength, while variable, were often present. History or evidence of a primary focus of infection was elicited in 78 per cent of cases and was absent in 22 per cent.

In every instance in which the records were complete, there was tenderness, graded from slight to marked, over the involved side.

Results of analysis of urine from the bladder were essentially negative in 25 of the 36 cases. The average leukocyte count was 17,400 in the 20 cases in which it was recorded, the maximal count was 28,600, the minimal, 9,400. In only 2 cases was it less than 10,000. Results of culture or examination of a smear of pus obtained from the carbuncle at operation were recorded in 28 cases. In 27 of these, some strain of *Staphylococcus* either was present in pure culture or predominated.

Of the 23 cystoscopic examinations made, the results of 13 were without significance, and 10 disclosed pus or bacteria in the renal specimen. Renal function was normal on the affected side in 14 cases, diminished in 7 and not recorded in 15.

In regard to the roentgenographic data, the series of Spence and Johnston differed markedly from that of Graves and Parkins. In 66 cases in the latter series there were only 15 abnormal pyelograms while in 36 cases in the series of Spence and Johnston, 22 pyelograms were abnormal and in only 4 instances were normal pyelograms obtained.

The treatment of patients having this condition is surgical. On reviewing the results of treatment in this series, the distinct impression is gained that as a general rule, unless more than a third of the kidney

²¹ Spence, H. M., and Johnston, L. W. Renal Carbuncle. Case Report and Comparative Review, *Ann Surg* 109:99-108 (Jan) 1939.

is involved, conservative procedure is preferable as the first step, and is more often than not sufficient

Thirty-five patients were operated on in Spence and Johnston's group of 36, the exception being a patient dying of cerebral abscess, on whom necropsy was performed. Primary nephrectomy was carried out in 17 cases, with 1 death, possibly resulting from disseminated military tuberculosis three months after operation. Incision and drainage of the carbuncle were performed in 9 instances with no fatalities. Partial or complete excision or enucleation of the lesion was performed in 6 instances, with 1 death resulting from lobar pneumonia. In 1 of these cases nephrostomy was performed when a calyx was broken into. Two patients had drainage of a perinephric abscess without recognition by the surgeon of the presence of a carbuncle, the patients failed to improve, and later secondary nephrectomy was performed. In 1 case the carbuncle was treated by electrocoagulation, but the patient later required nephrectomy. In all, 52 per cent of the patients were originally treated by conservative surgical operation.

Hypertension—Crabtree²² discussed cases of unilateral infection of the urinary tract in which the patients either were cured of their hypertension or were markedly benefited by removal of the infected kidney. These cases are of particular interest because they do not represent terminal conditions, the specimens removed for study were pathologic specimens obtained at operation and not specimens taken at necropsy, with terminal alterations. The fate of the other kidney will in some, if not in all, instances be determined eventually.

Crabtree collected 5 cases of unilateral destructive renal lesions associated with hypertension in which the patients improved after nephrectomy, and he added a sixth case.

Crabtree stated that from a survey of the data pertaining to this group of cases it may be concluded that the term "cure" after operation should be used with reservations. Whereas in 3 cases the data seem to indicate complete recovery for periods as long as two, fifteen and twenty months, respectively, in the other cases return of hypertension is known to have occurred in two months and there is no certainty about the freedom of the remaining kidney from permanent damage at the time the operation was performed.

Crabtree concluded that there is a small group of cases in which patients are both children and adults and in which hypertension associated with unilateral renal disease either retrogresses so far as the patient has been followed or is greatly, although temporarily, relieved by nephrec-

²² Crabtree E. G. Hypertension in Destructive Infected Unilateral Lesions of the Kidney. *Tr. Am. A. Genito-Urin. Surgeons* 31: 299-319, 1938.

tony The constant observations in these cases are obstruction to the outflow of urine and damage to the renal parenchyma, which in all cases is extensive and hypoplastic in type, with involvement of the substance of the cortex of the kidney, either in infective processes which are healing or in still active processes with abscesses. In 5 of the six cases reported by Ciabtree, bacteria were still present in the infected kidney at operation. No single type of infecting agent was encountered. Both coccic and bacillary types of infection were found.

Striking recessions in blood pressure followed nephrectomy in all 6 cases. The lapse of time was not sufficient in 4 cases to allow speculation as to outcome. The decrease in blood pressure persisted for two months in 2 instances, fifteen months in another case and twenty months in the fourth. In 1 of the cases of two months' duration the concentration of nonprotein nitrogen was elevated, there was an increase in blood pressure, and the concentration of nonprotein nitrogen fluctuated with it. Whereas both the blood pressure and the blood chemistry were normal, the excretion of phenolsulfonphthalein by the remaining kidney was not normal.

"Cure" is not necessarily the proper term to apply to results of treatment of these patients. Whether or not in the end cure is accomplished in any instance, nephrectomy appears to be a good therapeutic measure for prolongation of life of the patient.

Decapsulation—Linder and Sarre,²³ using Rein's thermostromuhr, examined the renal blood flow in dogs after experimental mercurial poisoning and noted the reaction of the blood flow after renal decapsulation. The renal blood flow was reduced to 40 per cent of its original rate three hours after the intravenous administration of 7 mg of mercury bichloride per kilogram of body weight. When the kidney was decapsulated at once the blood flow was not reduced, but remained constant. Its decrease was therefore caused by mechanical factors, probably the swelling of the tubular epithelial cells. In consequence, Linder and Sarre recommended early decapsulation.

Nephrobronchial Fistula—Lee²⁴ reported 2 cases of nephrobronchial fistula. He stated that nephrobronchial fistula, although it is a rare condition, should be considered when a patient having renal disease or perinephric abscess is afflicted with severe cough which is productive of purulent sputum. Drainage of the perinephric abscess relieves the cough and sputum and cures the pulmonary involvement.

23 Linder, F, and Sarre, H. Dekapsulation und Durchblutung der Niere, *Ztschr f urol Chir u Gynak* 45 40-48, 1939.

24 Lee, H P. Nephrobronchial Fistula, with Reports of Two Cases, *J Urol* 41 117-125 (Feb) 1939.

Pyelonephritis—Braasch²⁵ stated that since pyelonephritis is often secondary to infection in the lower portion of the urinary tract, treatment must be directed to this source in order to prevent recurrence.

Elimination of pus from the urine and cessation of symptoms do not necessarily mean that infection has been completely eliminated. Repeated cultures must be made subsequently to insure recovery.

Recent developments in chemotherapy have provided physicians with two compounds which are much more efficacious in the treatment of infection in the urinary tract than any other drug previously employed and often produce miraculous results. They are sulfanilamide and mandelic acid. Compounds of sulfanilamide should be used more frequently than at present as a preventive of infection such as occurs when post-operative retention of urine is present. The bactericidal influence of sulfanilamide in small doses is employed for this purpose, and also in other types of urinary infection.

With the increasing efficacy of chemotherapy and the development of special vaccines, it may be predicted that primary pyelonephritis will be largely limited to the acute and subacute stages of the disease and that chronic pyelonephritis with its complications will develop only occasionally. Adequate treatment of it will however entail a thorough study of all the factors involved, including the bacterial, physiologic and anatomic factors.

Adrenal Tumors—MacKenzie and McEachern²⁶ described a case of paroxysmal hypertension induced by adrenal pheochromocytoma. A man of 29 had suffered attacks of increasing severity for eighteen months. Attacks lasted three to twelve minutes and were characterized by nausea, substernal distress, generalized and localized headache, tremor, pallor and numbness of the extremities and were followed by exhaustion. During attacks there were a great increase in blood pressure, slowing of the heart rate, disappearance of the radial pulse, decrease in dermal temperature, lymphocytic increase in the blood stream and glycosuria. In the intervals between attacks the blood pressure was normal, and there was no cardiovascular abnormality. Plain roentgenograms, intravenous pyelograms and massage over the adrenal glands failed to demonstrate presence of the tumor. Surgical exploration of the region of the left adrenal gland revealed no tumor. Exploration on the opposite side showed an encapsulated pheochromocytoma the size of a golf ball (weight 24 Gm), which was removed.

²⁵ Braasch, W. F. *Pyelonephritis and Its Treatment*. Surg. Gynec. & Obst. 68: 534-539 (Feb. 15) 1939.

²⁶ MacKenzie, D. W., and McEachern, D. *Adrenal Pheochromocytoma. The Syndrome of Paroxysmal Hypertension. Report of a Case and Relief by Operation*. Tr. Am. A. Genito-Urin. Surgeons 31: 127-154 1938.

from the adlenal medulla. An extract of it contained a large amount of epinephrine (0.38 Gm per hundred grams of tumor). No further attacks occurred after operation, and eleven months later the patient reported that he was entirely well.

Data are recorded in 20 cases in which patients were subjected to operation. Five patients died, and 15 were completely relieved. Evidence indicated that the paroxysms of hypertension were due to the intermittent hypersecretion of epinephrine by the adrenal chromaffin tumor.

Cahill²⁷ stated that what are described as "adrenal cortical syndromes" are more frequently encountered without than with an accompanying demonstrable adlenal tumor. The syndromes are often characterized by sexual changes in the direction of adult masculinity in the female (androtropic), and rarely by feminization of the male (gynecotropic). They are also characterized by more than normally rapid advancement toward maturity in the young (prematurity) or the appearance of more advanced age in the mature (presenility). In some patients there are also present general metabolic changes, more particularly in the plasma, skin and adipose tissue, and in the psychologic status. In some instances one type may predominate, in others all trends may be present.

For diagnosis, visualization of the adrenal glands by the injection of air and roentgenographic examination was used to differentiate between tumorous and nontumorous involvement.

Excretion of androgenic substances in the urine seems to vary with the extent of sexual change and may be present both in patients not having a tumor and in those having a tumor, and may be reduced after removal of the tumor or, if no tumor is present, after diminution of the adrenal cortex. A specific hormonal substance may be excreted in the presence of some tumors.

The operative risk in the surgical treatment of androtropic tumors is less than that accompanying treatment of tumors characterized by marked metabolic changes in the patient, because in the latter instance atrophy of the opposing adrenal gland appears to be frequent. The atrophy may be prevented by preoperative therapy.

Removal of the tumor produces a symptomatic cure, but does not correct the fixed anatomic changes, and hirsutism of the face often persists.

There are apparently temporary sympathetic changes in the neural sphere in patients who do not have a tumor, following operation.

²⁷ Cahill, G. F. Adrenal Cortical Syndromes and Adrenal Tumors. *Fr. A. Genito-Urin. Surgeons* **31** 111-126, 1938.

decrease in the amount of the adrenal cortex. Changes in bodily contour and the mammae have been noted, but none in hirsutism, the genitalia or the voice.

Ureteral Inflammation—Hager and Boetticher²⁸ reported a case of membranous inflammation of a ureteral stump with spontaneous rupture. A woman aged 60 had had vesical trouble for many years. The condition had recently become worse with a sense of painful pressure, dribbling and burning on urination and at times she had had an incessant desire to urinate. This sensation was often followed by the passage of large pieces of tissue, with considerable relief. The right kidney had been removed twenty-one years previously, and right oophorectomy and appendectomy had also been performed. Results of the general physical examination were essentially normal. Examination of the external genitalia revealed a solid tenacious, grayish brown tissue protruding from the urethral meatus. This tissue was removed and was found to be an aggregation of elastic-like tissue.

Cystoscopic examination revealed diffuse cystitis. Both meatuses were in normal position. Clear urine in normal spurts was seen issuing from the left ureter. Hanging out of the right ureteral orifice was an irregular white mass, which could be made to float with irrigating fluid. The appearance of this mass was much like that of the tissue that had previously been removed from the urethra. A catheter was passed up the right ureter for a distance of about 10 cm, with drainage of foul-smelling purulent material; the left ureter was catheterized, without difficulty and with rapid drainage. Through the catheter in the right ureter an opaque medium was injected which procedure showed a rather marked dilatation of the ureteral stump with inclusion of the original shadows. A diagnosis was made of empyema of the right ureteral stump, with membranous ureteritis.

The patient was readmitted on several occasions with somewhat similar symptoms. At her last entry, because of inability to remove the tenacious material with a cystoscopic rongeur, it was felt that irrigation of the bladder, together with instillation of sterile olive oil, would assist in expulsion of the mass. This was done, and after several days a large mass of tissue, measuring 4 by 3 cm, was passed. Severe pain in the lower right portion of the abdomen developed, together with a sore spot in the back over the region of the scar on the right side. Examination showed an inflamed, indurated portion, about 4 cm in diameter, in the region of the old surgical scar. With the patient under general anesthesia, about 30 cc of thick, foul-smelling material

²⁸ Hager B H and Boetticher E O. An Unusual Case of Membranous Inflammation of a Ureteral Stump with Spontaneous Rupture, *J Urol* **41** 151-156 (Feb.) 1939.

was aspirated, culture of which showed the presence of an anaerobic streptococcus. The abscess was then incised and drained, after which the patient became much better.

Most instances of empyema of the ureteral stump are associated with stenosis of the most dependent portion of the structure or with stone. In the case reported, judging from the size of tissue protruding from the ureteral meatus as well as from the ribbon-like coils of material accumulated in the bladder, an impediment to drainage did not seem to be a constant factor. Neither was any difficulty encountered in introducing catheters the length of the residual ureters of this patient.

Dilatation—In discussing dilatation of the ureters in children, Vermooten²⁹ emphasized Chwalla's discovery that at about the second month of embryonic life, at the moment the ureter separates from the wolffian duct, its vesical end becomes occluded by an epithelial membrane.

Attention was also directed to Brown's observations that in a mouse embryo metanephric secretion begins on the fifteenth to the sixteenth day, and that hydronephrosis and hydroureter develop, become evident by the seventeenth day and are well marked by the eighteenth day. Further, on the nineteenth to the twenty-fifth day, either the obstruction at the ureterovesical junction spontaneously disappears or hydronephrosis becomes an established fact. These observations on mice apparently confirm those of Chwalla on human embryos.

It was suggested that it is the pressure of the metanephric secretion in causing ischemia of the delicate membrane that is responsible for sloughing of the membrane and in that way permitting the secretion to pass into the bladder.

The presence of congenital valves, ureteroceles and "strictures" at the ureterovesical junction was readily explained by the fact that in certain instances the epithelial membrane may persist for an unduly long time.

It was pointed out that in interpreting the causative background of the various types of ureteral dilatation in infants and children the aforementioned anatomic and physiologic observations on embryos are of the greatest significance. These facts should also be borne in mind before the urologist commits himself to the diagnosis of such condition as "segmental neuromuscular imbalance of the lower third portion of the ureter."

Recommendation was made that destruction of the membrane, if it still exists, together with adequate ureteral dilatation, with or without

²⁹ Vermooten, V. A New Etiology for Certain Types of the Dilated Ureter in Children, *J Urol* 41 455-463 (April) 1939

ureteral meatotomy, is the most conservative as well as the only treatment necessary to correct the congenital deformity

If the process has proceeded so far that the ureteral musculature has been destroyed, the urologist cannot expect the ureter to return to normal by any operative procedure other than a plastic one

The sooner after birth the condition is recognized and corrected the greater will be the opportunity for an eventual return to normal

Transplantation—Higgins,³⁰ in discussing the transplantation of ureters in infants, stated that the infant tolerates surgical procedures well. This tolerance is attested by the results secured by operations for intussusception, hypertrophic pyloric stenosis, strangulated hernia, cleft palate and harelip.

As the child becomes older, recurring attacks of renal infection may eventually result in renal sepsis and death. Similarly, as months or years elapse, dilatation of the lower third portion of the ureters frequently occurs, which may render transplantation into the bowel technically difficult or impossible.

It is probable that the organisms present in the colon during early infancy are less virulent than those present in later childhood or adult life. When the operation is performed at an early period in life the child may develop normally from both the physical and the mental standpoint. Because of the unfortunate defect, the parents may become extremely attached to the child, if death should result from the operation, it is better for it to occur before such sentimental ties are established. For these reasons, Higgins expressed the belief that operation should be performed during the first few months of the patient's life. During the past year, this procedure has been carried out on 7 children less than 1 year of age, and the results have been entirely satisfactory.

After a period of preoperative preparation, operation is performed with the child under ether anesthesia and in the Trendelenburg position. The two stage operation, with employment of a modified Coffey I technic, is used. The right ureter is transplanted into the rectosigmoid portion of the colon, and approximately ten days later the left ureter is transplanted into the bowel. If the child's condition permits, the bladder is removed at the second transplantation, or this procedure may be deferred to a later time, when correction of the urethra is accomplished. The operation should extend down to the bowel. If anastomosis is performed with the bowel delivered into the incision, there is danger of kinking of the ureter, or too much tension may be exerted on the ureter when the bowel is replaced in its normal position. Instead of introducing the cut end of the ureters into the lumen of the bowel

³⁰ Higgins, C. C. Transplantation of Ureters in Infants, *J Urol* **41** 464-470 (April) 1939

as the first step in the transplantation, this should be deferred until after the anchoring and transfixing sutures have been placed, thereby anchoring the ureter and closing the trough in the wall of the bowel. The ureter is then introduced into an opening through the mucosa made by a spear-point scalpel, and the final sutures are tied. After this, a complete change of gloves by the operating team is advisable.

In Higgins' 7 cases, convalescence was unusually smooth and devoid of complications, except for impetigo in the case of 1 child and disruption of the wound in another. There was no mortality, all the children leaving the hospital in a satisfactory condition.

BLADDER

Vesical Tumor —McClelland³¹ discussed endometriosis of the urinary bladder. He stated that in most cases endometriosis follows a pelvic operation on the female organs. The symptoms are cyclic in occurrence, coming immediately before and during each menstruation. There are usually pain over the region of the bladder, frequency of micturition and pain at the end of micturition. Hematuria is not a symptom, but blood in microscopic quantities is found in the urine during the period.

The cystoscopic picture varies from localized reddening of the mucosa to bluish cysts. The cysts are contained in a puckered region of the bladder and are covered by mucosa. During the intermenstrual period there is a decrease in the size of the mass.

Treatment is directed to removal of the ovarian hormonal influence. Sterilizing doses of roentgen rays or surgical removal of the ovaries causes disappearance of these symptoms.

McClelland reported 1 case of the condition involving a woman of 41. She had had tenderness over the region of the bladder, in the midline. Four months previously she had had cesarean section for termination of a three months' pregnancy, with ligation of the tubes. She had moderate frequency and slight dysuria. At the first examination, cystoscopy revealed nothing abnormal. Later, cystoscopy revealed an area of redness in the right lateral wall of the bladder. Vaginal examination disclosed a small lump, the size of a walnut, lying to the right of the uterus. At operation the uterus and ovaries were involved by adhesions, but no evidence of endometriosis was observed in the peritoneal cavity. The peritoneum was then folded back, and a lump was felt in the region of the uterus. The lump was resected extraperitoneally. The pathologist's report showed this mass to be endometriosis of the urinary bladder.

This patient had had a pelvic operation which was followed immediately by vesical symptoms. A lesion was not seen inside the bladder.

³¹ McClelland, J. C. Endometriosis of the Urinary Bladder, *Trans. Am. Genito-Urin. Surgeons* **31**: 215-219, 1938.

until cystoscopic examination four years later, at which time a region of localized redness was noted. Later the bluish cystlike bodies were seen in the region of localized redness three years before. The absence of endometrial tissue in the peritoneal cavity led to a change of diagnosis during the operation and to resection of the localized lump in the bladder. If endometrial implants had been found, oophorectomy would have been sufficient and resection would not have been necessary.

Reynolds³² stated that the possibility of endometriosis of the bladder should always be considered in treatment of a patient suffering from frequency of urination, dysuria and hematuria. When this triad is cyclic and is exacerbated during the menstrual period, the necessity for urologic consultation should be brought to the attention of the general practitioner. If the urologist finds at cystoscopic examination that "blue-black cysts and endometriotic edema" are present the diagnosis of endometriosis of the bladder is certain. The method of choice in the treatment of vesical endometriosis is the induction of artificial menopause with roentgen rays. Surgical intervention, however, is indicated in the few cases in which the patient is considerably under the menopausal age and desires children.

Ewell³³ stated that small, nonspecific infective granulomas occurring in the urinary tract especially in the bladder and urethra, are frequent. A granuloma of the type and size of the lesion in the case reported by Ewell is rare, since a review of the literature does not disclose a similar case. In his case there had been seen at laparotomy, two years previously, extensive mesenteric lymphadenitis, the patient giving a long history of repeated attacks of tonsillitis which suggested that the tonsils were the focal point of infection and that the infection was an etiologic factor in both processes. Lesions of the type reported on by Ewell are of importance for several reasons, the chief being that they are frequently mistaken for neoplasms. Partial removal of the lesion and prolonged vesical drainage have produced temporary cure.

Colby³⁴ reported on a small group of malignant tumors of the bladder which were treated by supervoltage roentgen rays with a recently devised 1 000 000 volt generator. Although Colby considered the series inadequate for fair evaluation of this form of treatment, certain tumors appear to be profoundly affected by it and exhibit considerable regression. The portions of the tumor which project into the vesical cavity seem to be affected considerably more than those which have extended

³² Reynolds L. R. Endometriosis of Bladder, *J Urol* **41** 157-163 (Feb) 1939

³³ Ewell G. H. Non-Specific Infective Granulomata of the Bladder. Case Report *J Urol* **41** 627-637 (April) 1939

³⁴ Colby F. H. Super-Voltage Radiation in the Treatment of Bladder Tumors. *Tr Am A Genito-Urin Surgeons* **31** 227-244, 1938

through the vesical wall. Other tumors are affected little, if any, and are considered to be "radioresistant." It is not considered that super-voltage irradiation, in its present state, takes the place of operation in instances of circumscribed cancer which can be adequately removed. The dose thus far employed is probably considerably less than that which it is possible to use, but more experience is necessary before the dose can be standardized and its ultimate effect determined. Local and generalized untoward reactions are less than those accompanying lower voltages, and regression of the tumors is more evident.

Kretschmer and Doerhing³⁵ described a case of leiomyosarcoma of the urinary bladder. A summary of 14 cases of this condition was given, in 8 of which the diagnosis was positive and in 6 of which the tumor was described but was not diagnosed as leiomyosarcoma. Leiomyosarcoma usually afflicts patients under the age of 12 years or more than 45. In most instances, the lesion arises from the wall of the bladder. Metastasis is rare. Although in the case reported the tumor was enormous, Kretschmer and Doerhing called attention to the fact that the cystographic appearance of the bladder was normal. The correct diagnosis was not made until the specimen taken at necropsy had been carefully studied.

Priestley and Sawyer³⁶ discussed two stage total cystectomy for carcinoma of the bladder and reviewed several recent cases which had been reported in detail. They emphasized that total cystectomy can be performed with reasonable operative risk and that the results compare favorably with those of operative procedures for the removal of malignant growths from other organs in the body. When both ureters are transplanted into the bowel, the patient may lead a normal and comfortable life, providing the ureteral anastomosis functions satisfactorily. When, in exceptional cases, cutaneous ureteral transplantation is performed, the patient may not be so comfortable, but cutaneous transplantation of the ureters possesses no more undesirable features than does colostomy, which has been an accepted procedure for a number of years. Indications for total cystectomy are not as yet standardized. In the past the operation was reserved largely for patients who had high grade or recurrent lesions, and who undoubtedly had regional or distant metastases. In some cases in which the bladder was removed under these circumstances, satisfactory end results could not be anticipated, and were not obtained.

35 Kretschmer, H. L., and Doerhing, P. Leiomyosarcoma of the Urinary Bladder, *Arch Surg* **38** 274-286 (Feb) 1939.

36 Priestley, J. T., and Sawyer, M. H. Two-Stage Total Cystectomy for Carcinoma of the Bladder. Report of Two Recent Cases. *Proc Staff Meet Mayo Clin* **14** 65-68 (Feb 1) 1939.

Priestley and Sawyer expressed the belief that during recent years indications for total cystectomy have undergone a gradual change. At this time it is considered that the bladder may be removed wisely in some cases of very large low grade neoplasms or repeatedly recurring low grade neoplasms which cannot be controlled satisfactorily by less radical measures. High grade lesions which, to the best of the surgeon's knowledge, are still confined to the bladder may also be treated by complete removal of the bladder. Total cystectomy is performed preferably in two stages. Simultaneous bilateral ureterosigmoidostomy is performed as the first stage, and subsequently the bladder is removed. In exceptional cases, when cutaneous ureteral transplantation is performed, the entire procedure, including removal of the bladder, may be accomplished in one stage. The three stage operation is usually not desirable.

Lidzki³⁷ stated that dermoid cysts of the bladder are extremely rare. The number of cases thus far published does not exceed 15. These cysts may exhibit the symptoms of cystitis and offer as a pathognomonic sign the discharge of hairs on urination (pilimictio). Such a cyst may occur as a tumor protruding into the vesical cavity, or as a paravesical cyst which invades the bladder and communicates with it through a small channel, as was the case in the instance reported. The treatment consists in removal of the cyst, either by an intravesical or extravesical procedure or by a combined approach.

Lidzki reported a case of a woman aged 30 who suffered from intractable cystitis. Cystoscopic examination was impossible. Roentgenologic examination disclosed two shadows in the pelvis. Cystostomy revealed that one of the shadows corresponded to a stone, the other to a ball of hair. The latter lay in a diverticulum which represented a paravesical dermoid cyst that had opened into the bladder. The cystovesical, fistulous tract having been dilated and its contents removed, the cyst became practically obliterated.

Calculus—Twinn³⁸ reviewed the cases of vesical calculus involving patients treated at the New York Hospital since 1820. The operative mortality in the earliest period from 1820 to 1846, when perineal lithotomy was routinely employed, was 10 per cent. This mortality then increased greatly in the next two periods, between 1847 and 1866 and between 1866 and 1920, but since 1920 it has been only 5.4 per cent. The mortality from litholapaxy has consistently been too high, although it has decreased markedly since 1920.

³⁷ Lidzki, A. Dermoid Cyst of the Bladder. Case Report, *Ann Surg* 109:274-276 (Feb) 1939.

³⁸ Twinn, F. P. Surgical Removal of Vesical Calculus. An Experimental and Clinical Study, *J Urol* 41:360-365 (March) 1939.

Twinn expressed the belief that the choice of operation in cases of vesical calculi depends on the age and physical condition of the patient, the size and hardness of the stone, the presence or absence of urethral stricture or associated prostatic hypertrophy and the experience of the surgeon. More skill is required to perform litholapaxy properly than is needed for suprapubic lithotomy. Crushing possesses two advantages over cutting: (1) a shorter convalescence and (2) a lower mortality rate. At the New York Hospital the mortality rate for litholapaxy between 1847 and 1920 was very high (22 to 25 per cent). Since the organization of the Brady Foundation, in 1920, the operative mortality has decreased to 8.1 per cent, which is still much too high. The mortality for suprapubic lithotomy has been reduced to 5.4 per cent. It is believed that the operative mortality for patients subjected to litholapaxy has been excessive and that it can be greatly reduced by attention to details of proper technique.

A study of the 7 cases of death following litholapaxy among patients operated on from 1866 to 1920 shows the large part played by vesical traumatism, for 3, and probably 4, of these 7 deaths were caused by rupture of the bladder.

Stenosis of the Vesical Neck—Irwin³⁹ reported on the operative treatment of patients having stenosis of the vesical neck. In all, he reviewed 48 cases in which operation was carried out by means of a clamp-incisor.

The bladder is exposed by a vertical suprapubic incision $2\frac{1}{2}$ inches (about 6 cm.) in length, and is then opened. A finger of the surgeon's left hand, on which two gloves are worn, is passed into the rectum and presses the vesical neck forward, while the index or middle finger of the gloved right hand is pushed through the vesical neck into the prostatic portion of the urethra. The finger of the right hand is now forced down in front of and below the posterior part of the vesical sphincter, and continued backward below the anterior part of the trigon. The clamp-incisor, which Irwin designed in 1929, is applied, and the blade is pushed down the grooves to the end of the instrument. In this way, the posterior part of the internal sphincter and the center of the trigon for about 1 inch (2.5 cm.) are not only divided but also thoroughly crushed on each side of the incision. After division of the sphincter and the adjacent part of the trigon, the cut edges are drawn back, leaving a large opening in the vesical neck and a wide vertical gutter, thereby causing the outlet of the bladder to be situated on a much lower plane.

39 Irwin, W. K. The Operative Treatment of Stenosis of the Vesical Neck. *Brit J Surg* 26:764-767 (April) 1939.

Irwin listed the advantages of this technic. A short suprapubic incision is sufficient. The operation can be performed in two stages, the subsequent division of the sphincter and trigon being carried out without enlarging the preliminary opening made during cystotomy. The method is simple and the operation is quickly performed. The procedure is safe and free from postoperative complications. There need be no fear of hemorrhage or sepsis. The treatment is curative, in this series of 48 cases. Irwin did not see any patient who had recurrence of the obstruction at the vesical neck. If there is any adenomatous tissue in the prostate gland, it can be enucleated during the course of the operation.

Cystostomy—Kevser⁴⁰ described a simple technic for incising the bladder suprapubically for drainage. He makes a 1 inch (2.5 cm) incision 1 inch above the symphysis, proceeding with the use of local anesthesia. After blunt separation of the muscles and transversalis fascia, a large Hirschman anoscope is introduced. With reflected light, the anoscope provides a 1 inch circular field through which the peritoneal fold is dissected upward with a Kuttner roll until the wall of the bladder is exposed. The bladder has been previously distended with a solution of methylthionine chloride U. S. P., the site of puncture is accurately located by means of an aspiration syringe. This region is seized with Allis clamps and the portion of bladder held between these clamps is incised sufficiently to admit the introduction of a no. 24 F catheter.

If severe infection exists the operation is carried out in two stages. At first the wall of the bladder is exposed as described previously and the region is packed through the anoscope with acriflavine gauze. After twenty-four to seventy-two hours the gauze is removed and two narrow Richardson retractors are placed to spread the incision and bring the bladder into view, at which stage it is perforated and the drainage catheter is placed in position.

In closing the incision one stitch may be placed inferiorly, between the bladder and the fascia above the symphysis, closing the space of Retzius. Through and through silk worm sutures, including muscle, fascia and portions of skin on each side, one above and one below the catheter, close the wound and complete the operation. No other drainage is used.

The operation as performed in 7 instances has been shown to be of advantage, since there was no shock, pain or elevation in temperature. It affords opening the bladder under vision with exposure of a minimal amount of raw surface to infection or urine. It also avoids possible

⁴⁰ Kevser, L. D. Suprapubic Cystostomy by an Endoscopic Technique, *J. Urol.* 41: 228-233 (Feb.) 1939.

perforation of the peritoneum or intestine. The procedure has not been attended by infection of the space of Retzius or perivesical infection with urine.

Transurethral Operation—Thompson⁴¹ presented a series of 24 cases of dysfunction of the vesical neck in women, in which 35 transurethral operations were performed.

The causative background of this disease is not definitely revealed by histologic study of the tissue removed by transurethral operation. The hypothesis that it is caused by fibrosis in the sphincteric region seems fallacious in view of the fact that a considerable amount of fibrosis is observed in normal tissue taken from this region. A possible explanation of the condition is that hyperplasia of the superficially lying epithelium of the vesical sphincteric muscle occurs and causes urinary retention.

The results of operation have been classified as excellent in 14 cases, good in 5 cases, fair in 4 cases and poor in 1 case.

Removal of tissue from the entire circumference of the vesical neck is necessary to obtain a good result in all but those exceptional cases in which incision alone may suffice.

Observation of the patient by the urologist for a number of years after operation is advisable, and treatment, including dilatation with a Kollmann dilator, will probably be necessary in some cases in order to maintain normal vesical function, the transurethral operation can be repeated with benefit if urinary obstruction recurs.

O'Connor⁴² stated that small vesicovaginal fistulas with healthy surrounding tissue will heal after electrocoagulation, if postural drainage can be maintained with an indwelling catheter for a sufficient period. The possibility of utilizing this method should receive more consideration, especially in the case of patients on whom unsuccessful surgical repair has resulted in a small lateral opening. The method obviously has no place in the treatment of fistulas of the floor of the bladder or in that of extensive defects of the tissues.

Sympathectomy—Nesbit and McLellan⁴³ stated that sympathectomy relieves vesical pain, not by removing the essential afferent pathways leading from the viscus but by relieving spasm of the internal vesical sphincter, and perhaps other parts of the vesical musculature. Certainly the one constant and predominating feature in all the cases of Nesbit and

41 Thompson, G. J. Transurethral Operations on Women for Relief of Dysfunction of the Vesical Neck, *J. Urol.* **41** 349-359 (March) 1939.

42 O'Connor, V. J. Non-Surgical Closure of Vesicovaginal Fistula. *Trans. A. Genito-Urin. Surgeons* **31** 255-259, 1938.

43 Nesbit, R. M., and McLellan, F. C. Sympathectomy for the Relief of Vesical Spasm and Pain Resulting from Intractable Bladder Infection. *Gynec. & Obst.* **68** 540-546 (Feb. 15) 1939.

McLellan's series was vesical spasm prior to operation. Likewise, the one constant postoperative result was relief from intolerable spasm and ease of urination.

It further appears evident that section of the hypogastric nerves alone, without the more extensive and hazardous division of the lateral sacral sympathetic nerves, provides relaxation of the sphincter adequate to relieve spasm of the bladder.

Since normal afferent components exist in the bladder after sympathectomy, it appears illogical to suppose that vesical pain resulting from a malignant growth would be relieved by this operation.

In conclusion Nesbit and McLellan repeated

1 The parasympathetic (sacral) pathways carry the essential afferent components of the bladder.

2 The sympathetic (presacral, or hypogastric nerves) pathways may or may not carry afferent pain components of the bladder.

3 Division of the presacral nerves provides relief of vesical spasm and pain resulting from intractable vesical infections.

4 Division of the lateral sacral sympathetics in addition to [division of] the presacral nerves accomplishes this same end but does not appear to be necessary or desirable.

5 Sympathectomy brings about the relief of spasmodic pain by relaxation of the vesical outlet and the detrusor mechanism; it does not render the bladder insensitive to pain of other origin.

6 Sympathectomy for the relief of vesical pain should be resorted to only [for] those patients [whose] pain is clearly demonstrated to result from spasm of the vesical outlet.

7 Sympathectomy was not shown to cure the lesions of Hunner ulcer in the cases here reported.

Incomplete Emptying—Kirwin and Hawes⁴⁴ stated that the amount of residual urine is never constant and under different conditions may vary considerably. Their experiments indicated that any male above the age of puberty may have residual urine if the bladder is overdistended. In the presence of intravesical or intraurethral prostatic intrusion, if the bladder is overdistended acute retention is likely to develop. The amount of residual urine cannot serve as an indication for the employment of any particular method of surgical intervention directed at the prostate gland. Demonstration of residual urine is not in itself sufficient indication for the performance of operations on the vesical neck. Determinations of the residual urine should be carried out with greater accuracy than is the usual practice at present.

⁴⁴ Kirwin T. J. and Hawes G. A. The Diagnostic Value of Residual Urine Estimation. *J. Urol.* **41**: 413-429 (March) 1939.

URACHUS

Cysts—Kantor⁴⁵ stated that the most frequent abnormalities of the urachus are anomalies in development and formation of cysts, which may at times be related to congenital defects. Long classified cysts of the urachus into four anatomic groups—those which communicate with the bladder, those which communicate with the umbilicus, those which communicate with the bladder and umbilicus, forming vesicoumbilical fistulas, and those which do not seem to communicate with either structure.

Kantor limited his study, for the most part, to cysts which do not seem to communicate with either the bladder or the umbilicus. Patients having such cysts frequently present the diagnostic problem of differentiation of a midline suprapubic mass which is only slightly movable.

The incidence of cysts of the urachus is rather low. In 1886 Lawson Tait presented 12 cases of suprapubic cysts, several of which were without doubt urachal in origin. All the cysts were described as lying extraperitoneally. In 2 of these cases excision was attempted, which resulted in immediate fatality. In the remainder, incision and drainage were effected, with no immediate mortality, although several deaths were noted later. Among the patients who lived, Tait did not describe any subsequent recurrences. He was probably the first surgeon to diagnose this condition preoperatively.

In reviewing the literature on cysts of the urachus, it is found that the diagnosis is usually made at operation. After the usual suprapubic incision, the mass is observed to be extraperitoneal, and its origin from the urachus is frequently obvious. Because of the conception held by some surgeons that complete extirpation is necessary for cure, Kantor described the following cases:

A girl of 2 years was moderately ill. In the suprapubic region, and extending midway to the umbilicus, was a round, tender, cystic mass the size of an orange. During the examination the child expressed a desire to void and passed a small amount of urine. A midline suprapubic incision was made into a cyst which contained about 8 ounces (237 cc) of thick, creamy pus. Evacuation of the contents revealed a smooth-walled cavity, from which a specimen for biopsy was taken. The cyst was drained. The interesting point in this case was that the wound healed completely and the child became well after simple drainage. Excision of the cyst was unnecessary. When the patient was seen at the follow-up clinic six months later, the scar was firm and there was no evidence of recurrence of herniation. The cure effected by this simple procedure was unquestioned.

45 Kantor, H. I. Cysts of the Urachus. Report of Two Cases. *Arch. Surg.* 109:277-285 (Feb) 1939.

Kantor reviewed 36 reported cases. In 7 cases cure followed incision and drainage of the cyst. In all but 1 case infection was present. Three instances of incomplete excision with cure were noted. No recurrences in these cases have been reported.

Four cases of fatality subsequent to excision are recorded. In 3 of these peritonitis was given as the cause of death.

Four cases of excision secondary to initial incision and drainage were reported. In 3 of these complicating features may have prevented normal healing.

In many of the reports technical operative difficulty was noted in cases in which primary excision was performed. Adherent peritoneum was frequently excised with occasional difficulty in closure. The bladder was opened in several instances. In 1 case reported attempt at excision would have been futile.

PROSTATE GLAND

Enlargement—Deming and Neumann,⁴⁶ in a study of the early phases of prostatic hyperplasia, concluded that the early change of benign enlargement of the prostate in man is primarily a multiplication of fibromuscular elements. It resembles in its early stages the uterine fibromyoma, which is derived from muscle cells of the uterus. Since the posterior portion of the urethra and the internal vesical sphincter contain muscle fibers which are derived from the same embryologic building material as that of the uterus, it is fair to assume that these two tumors have the same origin. It is probable that the solid nodule produces a stimulating and proliferating effect on the epithelium of the wall of the duct, causing the epithelium to invade the solid nodule and form glands within it. The fibromyomatous tissue is invaded and overgrown by a more rapidly growing duct and glandular tissue, with the result that the nodule in its later stages has the appearance of an encapsulated glandular tumor. Benign prostatic enlargements are not the result of hypertrophy, but are caused by true hyperplasia, derived from muscle fibrous tissue and ducts.

Davis⁴⁷ stated that, although resection is the shorter procedure, prostatectomy is both safer and surer. Resection usually takes less time than prostatectomy as measured by the number of days spent by the patient in the hospital, but not as measured by the number of days of convalescence or by actual operating time. Perineal prostatectomy is decidedly safer than resection in the hands of some surgeons, although there is no essential difference when the best available mortality figures for each procedure are compared. In good hands prostatectomy by

⁴⁶ Deming, C. L. and Neumann, C. Early Phases of Prostatic Hyperplasia, *Trans Am A Genito Urin Surgeons* **31** 339-350 1938.

⁴⁷ Davis, E. Prostatectomy or Transurethral Prostatic Resection. A Plea for the Selectionist. *J A M A* **112** 681-687 (Feb 25) 1939.

either route is suier than resection in that the majority of surgeons agree that enucleation gives more dependable assurance of complete and permanent symptomatic relief

Patients are well seived and good results are obtained by skilful extremists of both groups. The mortality rate and the functional results of transurethral resection bear a definite relation to the skill and experience of the surgeon. The consensus indicates that the public demand for transurethral resection is showing a tendency to decrease. The number of urologists who are tending to decrease their percentage of resections is distinctly greater than the number tending to increase this percentage.

The chief, if not the sole, advantage of resection in the best hands over perineal prostatectomy in the best hands consists in the saving of from nine to fourteen days of postoperative hospital care. Transurethral resection, after having passed through a typical cycle of trial and appraisal, including both abuse and overcorrection, is now approaching the final stage of stability, with a clearly defined field of usefulness.

Nesbit⁴⁸ stated that transurethral prostatectomy, when properly performed, shows to advantage over other types of prostatectomy in that it is accompanied by a very low mortality rate, lessened morbidity and a greatly reduced period of hospitalization. An important advantage to the patient is that he is saved the distress and discomfort attendant on the wounds incident to open operations.

Transurethral prostatectomy is a sound procedure which demands a high degree of technical skill for its proper execution. Any surgeon possessed of this skill can perform the operation with the expectation of obtaining excellent postoperative results. Such a surgeon will recognize the limits of his own dexterity and will perform the operation only in those cases in which he can expect to carry out a rather complete prostatectomy. Other cases he will reserve for more appropriate surgical procedures.

The able resectionist will guard his patients against morbidity and death from needless loss of blood and from sepsis, since these complications have been largely eliminated by modern surgical methods. He will prevent the occurrence of traumatic stricture as a devastating sequel to an otherwise satisfactory prostatectomy.

Refinements in technic and improvements in the surgeon's armamentarium have increased the scope of usefulness for transurethral prostatectomy and have tended to decrease the limitations on it.

Powell⁴⁹ stated that, notwithstanding the wide use of anterior pituitary-like gonadotropic substance from the urine of pregnant women

48 Nesbit, R. M. Some Refinements in the Technic of Transurethral Prostatectomy, *J. A. M. A.* **112** 687-689 (Feb. 25) 1939.

49 Powell, T. O. Precocious Hypertrophy of Prostate Gland in Male. Treatment with Gonadotropic Hormone, *J. Urol.* **41** 206-209 (Feb.) 1939.

in the treatment of boys having undescended testes, there have been no reports in which abnormal prostate glands developed in these patients

He reported a case in which a youth aged 17 was treated weekly for one year with a preparation containing the gonadotropic principle from the urine of pregnant women. The prostate gland as palpated per rectum and as seen through the cystoscope seemed definitely hypertrophied. There was 150 cc of residual urine. The symptoms were typical of prostatism, with the addition of frequent abnormal erections of the penis. The hormonal treatment had failed to cause the testes to descend, and orchidopexy had been performed, with success.

The condition of the patient was followed for two years, at the end of which time his symptoms had greatly subsided and cystoscopic examination revealed only a mild glandular bar at the neck of the bladder. There was no residual urine.

Powell concluded that on the basis of experimental information, it was the continued treatment with gonadoprostatotropic substance that caused the precocious hypertrophy of the prostate gland in this case.

On the basis of analysis of the blood of 73 patients, Boyd and Berry⁵⁰ obtained evidence of the presence of lipopenia in cases of prostatic hypertrophy. The feature of this lipopenia was a decrease of 30 to 40 per cent in the concentration of total lipids, total cholesterol, ester cholesterol and phospholipid in the plasma. There was no significant alteration in the lipid content of the erythrocytes. For 20 patients who had elevated concentration of blood urea the lipid values of the plasma were not significantly different from those of 20 other patients who had no elevation in the concentration of blood urea. The condition was termed the "lipopenia of prostatism."

In conjunction with the results of recent experimental studies of the endocrine glands which have been reviewed, this evidence indicates that enlargement of the prostate gland must be considered part of a general metabolic disturbance. Lipopenia may now be offered as an additional feature of prostatism. Determination of the concentration of cholesterol or phospholipid in the plasma may be used as an index of the efficacy of various forms of treatment other than prostatectomy.

Gundersen⁵¹ stated that a satisfactory result in treating the aged patient who has prostatic disease depends largely on the skill and experience of the surgeon. Urethral trauma must be minimized by shortening

⁵⁰ Boyd, E. M., and Berry, N. E. Prostatic Hypertrophy as Part of a Generalized Metabolic Disease. Evidence of the Presence of a Lipopenia, *J Urol* 41: 406-412 (March) 1939.

⁵¹ Gundersen, A. H. Management of Prostatic Disease in Persons Past Seventy-Five. A Report of Seventy-Five Cases with End Results, *I. A. M. A* 112: 833-835 (March 4) 1939.

the operating time, hemorrhage must be under control at all times. Supportive transfusions of blood should be given more frequently to old than to young patients. Whenever possible, the entire obstruction should be removed in one operation, a second resection is often poorly tolerated. Asepsis, adequate removal of all obstruction and meticulous care of the draining catheter are even more important in older than in younger patients. Gundersen expressed the belief that sulfanilamide is of value when given preoperatively as a prophylactic against infection. Despite the fact that men of more than 75 who have prostatic obstruction are precarious operative risks, resection offers them relief from suffering and a comfortable life so far as the bladder is concerned. There will always be a mortality, but with care and proper management the rate can be kept surprisingly low.

Of 12 patients with prostatic hypertrophy reported on by Moore, Keyes and McLellan⁵² who were treated by roentgen irradiation, 6 required prostatectomy within two years, 4 were either improved or in equilibrium with the disease after three years, 1 died of an intercurrent disease, and the fate of 1 is unknown. In 5 instances the prostate gland, studied histologically, revealed only minimal changes that might be attributed to roentgen irradiation. These changes were slight periacinar fibrosis and relative absence of lymphoid tissue and evidences of inflammation.

Belt, Ebert and Surber⁵³ described a new anatomic approach in perineal prostatectomy.

A curving transverse perineal incision, 1.5 cm from the anal mucosa, exposes the delicate fibers of the median raphe. These fibers are cut, revealing the arching fibers of the external rectal sphincter muscle, which are raised to disclose the glistening longitudinal muscular layer of the rectum. The anal canal and rectum are depressed and pushed backward, defining the central tendinous plane of the perineum. The areolar tissue and tendinous portion of the rectourethralis muscle, joining the rectum to the base of the perineal membrane, are snipped through revealing the anterior free borders of the levator ani muscles and the flat sheath of the rectourethralis muscle. The rectourethralis muscle is split medially and is retracted laterally with the levator ani muscles exposing the tough, white, shining fascia of Denonvilliers covering the posterior surface of the prostatic capsule. By using, therefore, the cleavage plane present between the external sphincter ani muscle and the longitudinal

52 Moore, R. A., Keyes, E. L., and McLellan, A. M. Histologic Studies of the Effect of Irradiation on Hypertrophy of the Prostate, *Trans Am Assoc Genito-Urinal Surgeons* **31** 371-382, 1938.

53 Belt, E., Ebert, C. E., and Surber, A. C., Jr. A New Anatomic Approach in Perineal Prostatectomy, *J Urol* **41** 482-497 (April) 1939.

muscle fibers of the rectum, the capsule of the prostate gland is exposed bloodlessly and without cutting a nerve

Preoperative Mortality—Engel⁵⁴ called attention to the preoperative mortality accompanying prostatic obstruction. Forty patients or 74 per cent of 54 persons studied, Engel felt, died unavoidably, while in the case of 14 patients, or 26 per cent, death might have been prevented. This study emphasizes the potential danger attendant on the first catheterization of a patient suffering from acute urinary retention, a danger which those of the general medical profession must not ignore. Engel condemned use of the indwelling catheter as a routine method of preoperative drainage; he has reduced the preoperative mortality by substituting suprapubic puncture or regular intermittent catheterization. The preoperative methods outlined have not only reduced the preoperative mortality and morbidity, but have also resulted in a smoother postoperative convalescence and a reduction in the operative mortality.

Tumors of Connective Tissue—Wyler⁵⁵ described leiomyoma of the prostate gland afflicting a man aged 37. The history and symptoms were similar to those occurring in the presence of benign hypertrophy of the prostate gland. Perineal prostatectomy was performed. Microscopic observation did not show any signs of malignant degeneration, and the patient had not had recurrence two years after prostatectomy. This is the fourth case of true leiomyoma reported.

Smith and Mintz⁵⁶ stated that rhabdomyosarcoma of the prostate gland is a rare disease. Twelve cases have been found in the literature, and Smith and Mintz reported an additional case. In 49 per cent of the cases the tumor involved children less than 10 years of age, in all but 1 case the patients were less than 32 years of age. The meager evidence at hand tends to prove that rhabdomyosarcoma is very radioresistant. The tumors tend to recur locally and in the terminal stage metastasize by cellular dissemination through the blood. No instance of cure has been reported.

Sarcoma—Stirling and Ash⁵⁷ added to the 132 cases of sarcoma of the prostate collected by Lowsley and Kimball. They summarized the data of 35 recently published cases and added 5 cases of their own. The data were discussed briefly from the standpoint of the clinical

54 Engel W J. Preoperative Prostatic Mortality, *J Urol* **41** 505-514 (April) 1939

55 Wyler, J. Leiomyom der Prostata, *Schweiz med Wchnschr* **69** 339-340 (April 15) 1939

56 Smith, G G, and Mintz, E R. Rhabdomyosarcoma of the Prostate in a Boy Seven Years of Age. Review of the Literature. *Tr Am A Genito-Urin Surgeons* **31** 351-362, 1938

57 Stirling W C and Ash I E. Sarcoma of the Prostate, *J Urol* **41** 515-533 (April) 1939

picture and treatment, and more extensively from that of pathologic changes Stirling and Ash reached the following conclusions

1 Sarcoma of the prostate gland is not necessarily a tumor of early life

2 The diagnosis is easier in the earlier age groups because of the diminished likelihood of the presence among such patients of carcinoma and benign hypertrophy

3 Sarcomas in the earlier age groups are more malignant, metastasizing more freely and running a more fulminant course

4 In all age groups sarcomas of muscular origin are the most common, and the existence of primary lymphosarcoma of the prostate gland has not been proved It is likely that a number of the tumors reported as round cell sarcomas are in reality undifferentiated small cell carcinomas

5 While treatment is still of little avail, it is felt that, particularly in older patients, prostatectomy is most important if it can be carried out before metastasis has occurred

6 The symptoms are largely those of urethral and rectal occlusion, none being of much aid in differential diagnosis

7 In the old patient the prostate gland is firm, smooth and difficult to differentiate from a gland which has undergone benign hyperplasia, in contrast to the fixed, hard, nodular prostate gland invaded by carcinoma

8 Although in the presence of metastasis death can be attributed directly to the tumor, in the majority of cases death is caused by secondary complications, chiefly urinary obstruction and infection, as also is true in cases of benign hypertrophy of the prostate gland and carcinoma of the bladder

Massage and Blood Pressure in Cases of Prostatic Infection—Hammer and Schulte⁵⁸ stated that certain patients exhibit mild or marked vasomotor collapse after prostatic massage In order to determine what physiologic changes are responsible for this occasional development, observations were made on the pulse rate and blood pressure of 378 unselected patients In this series only 38 patients had lesions of the prostate gland other than prostatitis There was no significant difference in the vasomotor response, regardless of the condition in the prostate gland Likewise, differences in the observation depending on posture of the patient were negligible

In 4 of the 378 cases syncope occurred after massage of the prostate gland The average blood pressure prior to massage in these 4 cases

⁵⁸ Hammer, H J, and Schulte, T L Blood Pressure Changes Produced by Prostatic Massage, Proc Staff Meet, Mayo Clin 14 13-15 (Jan 4) 1939

was 125 mm of mercury systolic and 75 mm diastolic. After massage the average pressures were 62 mm of mercury systolic and 41 mm diastolic.

Of the entire group, 38 patients were less than 30 years of age, 304 were from 30 to 60, and 36 were more than 60. This last group was the smallest, but showed the highest percentage of extreme response (38 per cent). The first group had an average control blood pressure of 119 mm of mercury systolic and 76 mm diastolic, the second group, a pressure of 124 mm of mercury systolic and 79 mm diastolic, and the third group, a pressure of 138 mm of mercury systolic and 93 mm diastolic. After massage, the average blood pressures for the three age groups were, respectively, as follows: 123 mm of mercury systolic and 86 mm diastolic, 132 mm of mercury systolic and 86 mm diastolic and 157 mm of mercury systolic and 106 mm diastolic.

Of 378 cases, there were increases in systolic or diastolic pressure in 284 (75 per cent). Of the entire group, there were 89 cases (23 per cent) in which there was a decrease of both systolic and diastolic pressure. All patients had an increase in pulse rate, the average being 16 per minute. Of this series, there were 76 patients (20.1 per cent) for whom hypertension might be predicted on the basis of a hyperresponse to prostatic massage in both systolic and diastolic blood pressure. Thirty-one patients in the series had essential hypertension. Of these, 18 patients (58.06 per cent) showed an extreme response, and only 3 patients exhibited minor decreases in both systolic and diastolic pressure.

In the 50 cases in which both prostatic massage and the cold pressor test were used, it was found that as a result of massage the average increase in systolic pressure was 22 mm of mercury and in the diastolic 20 mm of mercury. The average increase in pulse rate was 23 per minute. As a result of the cold pressor test, the average increase in systolic pressure was 19 mm of mercury, and in the diastolic, 16 mm of mercury. The average increase in pulse rate was 3 per minute. After massage 18 patients (36 per cent) had a hyperresponse, although in the cold pressor test there were 13 patients who had such a response. In the 13 cases in which there was a hyperresponse to the cold pressor test there also was a hyperresponse to massage.

The considerable elevation in blood pressure produced by prostatic massage in patients who had essential hypertension should be taken into consideration when such a procedure is undertaken.

TESTICLE

Tumors—Quimby⁵⁹ reviewed a series of 26 cases of testicular tumor reported from the urologic clinic of the Peter Bent Brigham Hospital.

⁵⁹ Quimby, W. C. *Clinical Aspects of Testicular Tumors*, Rhode Island M. J. 21: 119-121 (Aug.) 1938.

He stated that although in earlier years in instances of testicular tumor attempts were made to remove the region of lymphatic drainage in the abdomen, as an addition to orchidectomy, further anatomic knowledge of the region of lymphatic drainage has shown this procedure to be hardly feasible. Also, during the past decade it has been shown definitely that many of these tumors are especially sensitive to irradiation with high voltage roentgen rays or with radium. The accepted treatment today, therefore, is that of immediate removal of the testicle by section of the spermatic cord at the external inguinal ring, followed by one or two courses of high roentgen voltage irradiation applied to the whole abdomen as high as the level of the kidney.

Seven of Quinby's patients were living without apparent recurrence, 2 of them after a period of as long as nine and ten years, respectively, 2 were living, but since operation had had metastases which had been caused to disappear with high voltage roentgen ray therapy, 2 died, 1 five and the other eleven years, after the onset of cardiorenal or circulatory disease not related to the neoplasm. Thus, there were 11 patients of 26 who were living or who died without recurrence. Fifteen patients died—2 of them with recurrence of the "hurricane type"—within two months of operation, and 6, within one year after operation. Four patients survived operation for from one and a half to four years, dying of recurrence.

Of the surviving patients, 4 had no treatment other than orchidectomy, and were still well.

Roentgen ray therapy was administered intensively, without effect, to 12 of the patients, who died. For 2 patients roentgen ray therapy seemed to have held the disease definitely in check.

Mackenzie and Ratner⁶⁰ stated that tumors of the testis metastasize early by the way of the lymphatic vessels and blood vessels. The lymphatic spread is achieved along the glands of the spermatic cord, up along the retroperitoneal group of glands, thence to the mediastinal glands and finally to the supraclavicular region on the left side. Metastases via the blood stream probably result from invasion by the tumor of the pampiniform plexus of veins. Metastases from tumors of the testis occur long before there is any clinical evidence of them.

MacKenzie and Ratner expressed the belief that every patient having a tumor of the testis must be examined periodically, at least three times a year, and that a careful search must be made for metastases, including roentgenologic examination of the thorax. If a secondary growth is discovered immediate irradiation must be instituted.

⁶⁰ MacKenzie, D. W., and Ratner, M. Metastases from Tumors of the Testis. *J. Urol.* **41**: 592-608 (April) 1939.

A quantitative estimation of the concentration of the follicle-stimulating principle in the urine should be made in every case of suspected tumor of the testis, and periodically in the case of every patient known to have had a testicular growth. A negative result, however, does not exclude the presence of testicular growth or metastases.

The prognosis for a patient having a testicular growth must be determined not only by the biologic response of the tumor to irradiation, but also by the clinical picture and by a careful histopathologic study of the growth.

Intensive irradiation should be administered in all cases of metastases. If the tumor is radioresistant, prolonged irradiation with smaller doses, according to the method of Coutard, is recommended.

Since the use of high voltage roentgen ray therapy, the prognosis and outcome in cases of tumors of the testis, including even those in which there are metastases, have been better.

Dean⁶¹ stated that in a series of 39 patients seen within three months of the first symptom, he found metastases in 67 per cent. Although this figure demonstrates exceedingly high malignancy, study of approximately 600 patients who had teratomas led him to believe that the fulminating condition, in which small primary tumors throw out showers of metastases, especially through veins, is an exceptional deviation from the average natural history of the disease and that in the majority of cases there is an opportunity for application of effective treatment before metastases become too widespread.

While it cannot be told how long the testicular tumor has been growing before the patient realizes that something is amiss, it is interesting to note that after discovery few other tumors cause patients to seek medical advice more promptly than a testicular tumor. Nearly 70 per cent of Dean's patients consulted physicians within four months of the first symptom. This is remarkable, for the patients were mostly young men in otherwise good health and the tumors rarely caused them discomfort. On the other hand, after these patients had been seen by physicians the average loss of time before the correct diagnosis was made was six and a half months. In this delay, Dean asserted, lies the reason for the majority of tragedies from teratomatous growths. Fifteen years ago errors of diagnosis made little difference in a case of teratoma, because there was no proved effective therapy to be instituted, but now that irradiation has demonstrated its value and high voltage roentgen ray units are commonly available, a heavy responsibility rests on the physician who first sees a young man having testicular enlargement. Every intrascrotal swelling should be examined with the

61 Dean A. L. in discussion on MacKenzie and Ratner⁶⁰

possibility in mind that it may be a teratoma, and because teratoma is by far the most serious disease of the testis, it should be ruled out first

It is of the greatest importance to have the upper part of the body completely uncovered whenever the physician examines an intrascrotal swelling. It may be impossible to determine the nature of an enlarged testis by inspecting or palpating it, but if a mass can be felt in the abdomen on the same side, or in the epigastrium or left supraclavicular fossa, little doubt remains as to the diagnosis. Also, with the chest uncovered, the physician may occasionally discover gynecomastia, a significant clue to abnormality of internal secretion. Two observations have been of especial value in diagnosing the primary growth. 1. Tumorous tissue is usually denser and heavier than normal testicular tissue, a quality which has been detected when the suspicious nodule was approximately 1 cm in diameter. 2. In Dean's group of cases teratomas were most commonly mistaken for hydroceles. These conditions can readily be differentiated by noting that the swelling produced by a tumor ends with a cleancut line of demarcation at the upper limit of the growth, whereas fluid of a hydrocele extends upward in most cases as far as the base of the penis and creates the impression of a shortened or partially retracted penis. In all cases, roentgenograms of the thorax should be taken, in search of blood-borne metastases. These are usually found first in the lungs, where they stand out as dense, clearcut shadows, each perfectly circular because it is shaped by the vein in which it grows. In a large group of patients with metastases it was found that one third had blood-borne extensions in the lungs. Next in frequency to metastases in the lungs were venous metastases in the brain. As yet there is great difficulty in demonstrating these tumors roentgenographically, although after symptoms arise they usually can be localized by neurologic examination.

The Aschheim-Zondek test, in Dean's opinion, is an unsafe basis for clinical procedures at present.

Cabot and Berkson⁶² reported a study based on an analysis of 363 cases of neoplasms of the testis. The mean age of these patients was 36.2 years, the age of the youngest being 17 months and that of the oldest 84 years.

Of the 363 patients, 148 were first examined at the Mayo Clinic, 215 came to the clinic only after they had been treated or a diagnosis had been made elsewhere, they were sent to the clinic primarily for irradiation, many of them having extensive metastases. Of the 148

62 Cabot, H., and Berkson, J. Neoplasms of the Testis. A Study of the Results of Orchidectomy, With and Without Irradiation, *New England J Med* 220: 192-195 (Feb 2) 1939.

patients first examined at the clinic, 142 were treated by orchidectomy, with or without irradiation. Of the 215 other patients, all were treated at the clinic by irradiation, and 165 of them had had operations elsewhere.

In 59.2 per cent of the 142 cases in which orchidectomy was done the tumors were classified as seminomas, in 34.5 per cent as adenocarcinomas of various forms and in 6.3 per cent as miscellaneous types of cancer.

The ten year survival rate of patients having seminoma was found to be relatively high as compared with what is, Cabot and Berkson stated, the commonly held opinion. Thus, 47.4 per cent of the patients were alive and apparently well ten years or more after treatment. This rate should be compared with the corresponding survival rate of the patients classified as having carcinoma, which was 26.4 per cent.

The survival rate of patients having seminoma is much higher than that of patients having carcinoma, at the end of five years being 67.7 per cent, as compared with 29.3 per cent.

Irradiation seems materially to improve the three and five year survival rates for patients having seminoma. Thus, of the patients treated by orchidectomy followed by irradiation, the survival rate at the end of three years was 80 per cent, as compared with 68.4 per cent of those not treated by irradiation. At five years the survival rate was 71 per cent of the patients receiving irradiation as compared with 58.8 per cent of those not so treated. Irradiation does not appear to have any important effect on the rate of survival for ten years or more. Of the patients treated by irradiation, 47.9 per cent lived more than ten years, as compared with 46.7 per cent of those not so treated.

Of these 142 patients, 6 lived twenty years or more, 2 had carcinoma and 4 seminoma, none was treated by irradiation.

Lewis and Priestley⁶³ stated that approximately 50 cases of bilateral testicular neoplasms are reported in the literature. They reported 2 recent instances which they encountered. One concerned a man 44 years of age who had noted simultaneous bilateral testicular enlargement two months prior to admission. Both testes were removed, and microscopic examination revealed bilateral carcinoma, grade 4, of the seminomatous type. No metastases were noted at the time of operation. Determination of gonadotropic substance in the urine by the Aschheim-Zondek technic revealed more than 66 rat units per liter of urine, an abnormally high amount. Roentgen therapy was administered. Two months later, grossly palpable metastases were present. The second case involved a man 58 years of age who had noted enlarge-

⁶³ Lewis, E. B., and Priestley, I. T. Bilateral Testicular Neoplasms. Report of Two Cases, Proc. Staff Meet. Mayo Clin. 13: 737-740 (Nov. 23) 1938.

ment of the left testis one year prior to admission. Orchidectomy was performed, and the specimen taken for biopsy proved to be carcinoma, grade 4, of the seminomatous type. Determination of gonadotropic substance in the urine by the Frank technic showed less than 20 rat units per liter, which is probably not an excessive amount. There was no evidence of metastasis. Roentgen therapy was administered. Four months after operation the right testis started to enlarge. Orchidectomy performed one month later revealed a grade 4 carcinoma of the seminomatous type in this testis. Further roentgen therapy was administered, although there was no evidence of metastasis at this time.

Ectopic Testes—Thompson and Heckel⁶⁴ stated that reports of the effect of the anterior pituitary-like principle from the urine of pregnant women in the treatment of undescended testes appear to be exaggerated. In 38 patients of all ages, descent of only 10 of 50 undescended testes, or 20 per cent, was produced, as compared with an average of 61 per cent of successful results reported in the literature. Descent did not occur in any instance in which the testis was intra-abdominal or deflected over the external oblique muscle.

It follows that in the majority of cases of true undescended testes operative procedures are still necessary because of mechanical factors which prevent descent. The value of this form of treatment depends on the importance of getting the testis into the scrotum as early as possible. If early descent is important, the management of undescended testes involves the intelligent combination of medical and surgical measures.

Treatment should be discontinued before genital growth becomes excessive.

Johnson⁶⁵ made a study of 544 cases of undescended testicle in an effort to obtain a standard by which the value of the two methods—surgical replacement and endocrine therapy—could be compared and a base line drawn. His study has resulted in an interesting group of figures, which may be of value in comparing future therapeutic results.

In the 544 cases of undescended testes, careful examination revealed bilateral undescended testes plus Frohlich's syndrome in 17 cases and unilateral undescended testis plus Frohlich's syndrome in 11 cases, or a total of 28 cases of associated Frohlich's syndrome. Undescended testis was associated with hernia in 13 cases, malnutrition in 5, hypospadias in 2 and congenital cardiac disease in 2.

In 5 cases endocrine products were injected. In all cases the testes failed to descend when treatment was declared adequate and when

64 Thompson, W. O., and Heckel, N. J. Undescended Testes. Present Status of Glandular Treatment, *J. A. M. A.* **112**: 397-402 (Feb. 4) 1939.

65 Johnson, W. W. Cryptorchidism, *J. A. M. A.* **113**: 25-27 (July 1) 1939.

injections were stopped. In 4 instances orchidopexy was performed for the purpose of placing the testis in the scrotum. In 10 instances it was performed in conjunction with the repair of definite hernia. A total, then, of 14 operations to replace the testis were performed by various surgeons.

In 13 of the 246 cases of bilateral undescended testes, the two testes did not respond to treatment in the same way. The testes descended spontaneously, but one preceded its fellow into the scrotum. When these 13 cases and the 14 cases in which operation was performed are eliminated, there remain 517 cases to be considered. At the end of the survey there were 217 cases in which the testes were still undescended or the patient was lost track of. Spontaneous descent, resulting in a normal testis as to size, consistency and position, occurred in 300 instances. 162 cases of bilateral and 138 cases of unilateral undescended testes. Between the ages of 11 and 13 years, the testes descended spontaneously in 174 patients without therapy of any kind.

Johnson expressed belief that it is time to reconstruct all the old ideas of surgical intervention. If operations "before 11" had been carried out in this group of patients, 232 useless and detrimental procedures would have been performed. These figures show that operation before the patient's sixteenth year would have been a mistake in most instances. After the fifteenth year there were still 16 instances of nondescent, and in 7 of these instances descent occurred spontaneously. Johnson suggested a new tenet: "Do not operate for undescended testis before the sixteenth year unless operation is indicated by some associated condition."

Torsion of the Pedicle of the Hydatid of Morgagni—Vaugh⁶⁶ described a gangrenous hydatid of Morgagni. The hydatids described by Morgagni as occurring in women are found near the infundibulum of the uterine tube. They usually have a pedicle and, like the hydatids described as occurring in the male, are usually small. Embryologically, they are believed to arise from the most cephalically situated portion of the wolffian duct. They are frequently seen during the course of pelvic operations and usually are thought to be of no clinical significance.

The patient described by Vaughn complained of persistent pain in the lower right abdominal quadrant. At operation a strangulated, gangrenous hydatid of Morgagni was observed hanging from the fimbriated end of the right oviduct. A small simple cyst was present in the right ovary. Otherwise the pelvis was normal.

⁶⁶ Vaughn J M. Gangrenous Hydatid of Morgagni. Proc Staff Meet, Mayo Clin 14 358-359 (June 7) 1939.

Torsion of the pedicle of such a hydatid is only occasionally encountered. In all, perhaps 18 cases have been reported.

The treatment of choice is ligation of the pedicle and excision. Prophylactic treatment, consisting of removal of all vesicular appendages with a pedicle encountered during laparotomy, to prevent a later accident, is highly desirable.

Torsion of the Appendix Testis—Randall⁶⁷ stated that gross anatomy recognizes that the sessile hydatid of Morgagni is the most constantly present rudimentary structure of that group of hydatids which owe their origin to vestigial remains of the müllerian duct or to embryonic faults of development. Situated on the anterior face of the superior pole of the testis, such a hydatid lies free of the overhanging globus major of the epididymis. Paradoxically, it is more often pedunculated than sessile, and its proper title is the "appendix testis."

The appendix epididymidis, often called the "stalked hydatid," is less constantly present, it arises from the tubules of the epigenitalis that do not form tubuli collectivi. It is said to contain plain muscle in its stalk.

Microscopically, the hydatid of Morgagni is covered with simple cylindric epithelium and is composed of loose fibrous tissue, with blood vessels and some plain muscle fibers, and usually contains remnants of a duct, lined with ciliated epithelium.

The clinical picture of torsion of the appendix testis has confusing points. The onset is practically always sudden, with unilateral acute pain. The pain is rarely so severe or so continuous as that accompanying acute infectious epididymitis. Complete torsion of the testis presents greater difficulty, although this condition is almost uniformly of greater symptomatic severity. Fortunately, differential diagnosis is not essential, since prompt operative intervention is the treatment of choice in both conditions. In cases of a few days' duration, the diagnosis becomes easier, and unless edema persists or a secondary hydrocele interferes, tenderness at the superior pole of the testis and just under the globus major of the epididymis is diagnostic.

The cause is still unknown. Certainly, infection plays no part. Trauma has been discussed, sudden or violent cremasteric reflex response has been suggested, but too many cases occur during ordinary play or occupation to allow such a conclusion to stand. In a few instances, such as those of torsion testis, the condition has occurred during sleep. It is suggested, apropos of the marked frequency of torsion during ado-

⁶⁷ Randall, A. Torsion of Appendix Testis, *Tr Am A Genito Urin Surgs* 31: 283-294, 1938.

lucence, that increased vascularity with testicular growth and development may play an important role. Certainly, persons in whom the hydatid has a greater pediculous development become potentially more liable.

The operation for treatment of torsion is so simple, and so devoid of any serious complications, that it should always be advised. Randall also advised fixation of the testis to the incision in the tunica vaginalis, during sewing up, as a step to prevent subsequent torsion testis, because the two conditions have been reported as occurring simultaneously. The question of conservative, nonoperative treatment is ill advised first, because no local treatment will relieve the distress; second, because detorsion and recurrent attacks are possible; third, because the nonoperative recovery may take longer than the operative removal and convalescence; and fourth, because the condition may give rise to hydrocele.

SCROTUM

Fat Necrosis—Hinman and Johnson⁶⁸ described 3 cases of acute fatty necrosis of the scrotum. All occurred in stout boys, before puberty, each of whom had been known previously to have had normally placed testicles. In 2 instances the lesion followed mild, but rather prolonged, trauma to the scrotum; in the third, the causative background was obscure. The onset was acute, accompanied by moderate pain and tenderness, with no other local condition (edema, ecchymosis), except a mass which could not be distinguished from the testes in the first 2 cases. Pathologically, the lesion resembled the fatty necrosis seen elsewhere. The condition was of interest chiefly because of its situation in the scrotum, which introduced a problem in differential diagnosis not previously encountered.

BARTHOLIN'S GLAND

Tumor—Simendinger⁶⁹ stated that only 38 cases of primary carcinoma of Bartholin's gland have been reported, and in these adenocarcinoma was the predominant type, in only 9 instances was the tumor squamous cell carcinoma.

In a review of the cases reported, it was found that the ages of the patients varied from 29 to 91 years. The average age in 30 cases in which the age of the patient was given was 51.6 years. The majority of carcinomas occurred in patients between the ages of 40 and 55.

⁶⁸ Hinman F and Johnson C M. Differential Diagnosis of Acute Fat Necrosis in the Scrotum. *J Urol* 41: 726-732 (May) 1939.

⁶⁹ Simendinger E A. Carcinoma of Bartholin's Gland. Report of a Case of Squamous Cell Epithelioma. *Surg, Gynec & Obst.* 68: 952-956 (May) 1939.

Infection is apparently not a predisposing factor in neoplasms of Bartholin's gland, since in only 2 cases was there a history of infection. Chronic infections of the gland are common and often lead to mistakes in diagnosis.

Carcinoma of Bartholin's gland is usually first noticed as a small, hard, painless, nodular swelling, lying deep in the labial fat. The lesion is usually movable at first, but sooner or later enlarges, according to the degree of malignancy present, and becomes attached to the surrounding tissues. The skin is usually not involved until later, so that when the tumor is first noticed the skin over it is freely movable. With enlargement of the tumor, pain develops, which is commonly referred to the coccyx and groin and is made worse by coitus and menstruation. Pain is usually the symptom which causes the patient to seek medical attention, and by the time such attention is sought the tumor is usually well established. As the skin becomes involved, the tumor becomes painful to the touch, and the skin is reddened and edematous.

The most important points in diagnosis are the age of incidence, the hardness of the tumor, with tendency toward fixation, pain and, later, edema of the vulva, failure to respond to treatment, and the results of biopsy.

Prognosis in cases of carcinoma of Bartholin's gland is unfavorable. The almost uniform failure of early diagnosis is the most important factor in the poor prognosis. According to Taussig, carcinoma of Bartholin's gland is almost uniformly fatal, as contrasted with the everting type of vulvar carcinomas arising from vulvar leukoplakia. Of 21 cases reported in which information was available, there was no recurrence in 1 in six years, in 1 in four years, in 5 in two years and in 4 in one year, in 5 cases the carcinoma recurred, and 5 cases were recorded too early after removal of the growth to make any report of absence of recurrence of value.

In the minds of most authors, the proper therapy for carcinoma of Bartholin's gland is a combination of irradiation and surgical intervention.

Simendinger reported 1 instance of the condition afflicting a woman of 74. Complete vulvectomy was performed, the patient was alive and well when last seen, eight months after operation.

HYPERPARATHYROIDISM AND UROLOGIC CONDITIONS

Chute⁷⁰ discussed the clinical aspects of 36 proved cases of hyperparathyroidism with reference to urologic conditions. In addition to general weakness, there were symptoms secondary to lithiasis in the

⁷⁰ Chute, R. Clinical Aspect of Hyperparathyroidism, with Special Reference to Urology, *J. Urol.* **41** 762-772 (May) 1939.

urinary tract and symptoms due to decalcification of the bony skeleton. Eighty-three per cent of patients had urinary lithiasis. In 53 per cent calculi were bilateral and in 73 per cent multiple.

Calculi are composed chiefly of calcium phosphate. Diagnosis is established by demonstration of an elevated concentration of calcium (more than 11.5 mg per hundred cubic centimeters) in the serum. The Sulkowitch test for the amount of calcium excreted in the urine is quick, easy and valuable.

Surgical resection is the only treatment that has been successful.

End results in this series of cases have been satisfactory. No new calculi have occurred in any instance.

The urologist must think of the possibility of the existence of hyperparathyroidism in every case of urinary lithiasis.

HEPATIC FUNCTION AND UREMIA

In the development and prevention of uremia the work of the liver is important. In some cases uremia can be combated successfully by increasing hepatic function. Such cases are characterized by a low xanthoprotein value for the blood serum. Babics⁷¹ tried a new drug biolipase, and obtained surprisingly good results. He asserted that this drug should be used more extensively in the preparation of patients for major operations, especially in the treatment of patients having uremia caused by prostatic obstruction.

UROLOGIC COMPLICATIONS IN MALIGNANT DISEASE OF THE RECTUM

Kickham and Bruce⁷² stated that the frequency of urologic manifestations in malignant disease of the rectum both in the natural course of the disease and as a result of treatment, demands that a definite plan of urologic investigation be included in the management of such rectal conditions.

The incidence of such manifestations increases with the advance of the malignant disease. The site of the primary lesion in the rectum is a significant factor. Although actual invasion of the urogenital organs may not be present, the normal physiologic processes may be affected by the encroaching malignant growth.

Obviously, as a result of injury to nerves during resection of the rectum interference with the normal physiologic state of the bladder

71 Babics A. Ueber die Behandlung der infolge chirurgischer Nierenerkrankungen auftretenden Uramie mit besonderer Berücksichtigung der Leberfunktion. *Ztschr f urol Chir u Gynak* 44: 465-475, 1939.

72 Kickham C I E and Bruce N H. Urological Complications in Malignant Disease of the Rectum. *J Urol* 41: 541-556 (April) 1939.

may occur in many patients, and signs and symptoms of neurogenic vesical dysfunction may be presented. Such dysfunction is chiefly the result of injury to the parasympathetic supply to the bladder. The trauma and manipulation to which the urogenital organs are subjected during rectal resection, as well as removal of the normal posterior supports of these organs, may be the cause of urinary disturbances, independent of injury to nerves. Militant measures must be employed to regain normal vesical function, to combat urinary infection and to conserve renal values.

It is only by painstaking preoperative and postoperative investigation of the urogenital tract that complications will be recognized and their associated effects averted. The necessity for close cooperation between the rectal surgeon and the urologist in the management of malignant diseases of the rectum is evident.

HORMONE THERAPY

Day⁷³ stated that in the presence of mild degrees of prostatic hypertrophy patients are afforded marked relief by the use of androgenic substances, especially testosterone propionate, even the distress caused by great hypertrophy of the gland is sometimes palliated for a considerable period. For patients who are under the age of susceptibility to prostatic hypertrophy, the intensive administration of androgen should not be instituted for too long periods. Androgenic therapy is in no sense to be considered a substitute for surgical treatment of major prostatic obstruction when the patient is a fair surgical risk. Before androgen therapy for patients having benign prostatic hypertrophy is commenced, there should be an adequate urologic examination and survey by a competent urologist, accessory urologic treatment should be instituted in conjunction with administration of androgen whenever indicated by the urologic survey. Synthetic testosterone is by far the preferred and most potent substance known and should be administered in adequate doses at sufficiently frequent intervals. For the sake of insurance, and in the present state of knowledge, it may be well to inject an extract of testicular tissue as an activator simultaneously with testosterone propionate.

Boshamer⁷⁴ stated that in Chinese medical practice the androgenic substances have played a great role throughout past centuries. Boshamer, who knows Chinese medicine by experience, found definite indications for the use of such substances in treating urologic patients. One of the

73 Day, R. V. Male Sex Hormone Therapy, *J. Urol.* **41** 210-219 (Feb.) 1919

74 Boshamer, K. Hormontherapie in der Urologie, *Ztschr. f. urol. Chir. u. Gynak.* **45** 16-30, 1939

chief qualities of such substances is their influence on congestive conditions of the prostate gland. This influence makes androgen especially suitable in the treatment of neuroses and hypertrophy of the prostate gland and chronic prostatitis. It relieves in a remarkably short time the phosphaturia usually accompanying chronic prostatitis. On the other hand, the indications for surgical removal of the hypertrophied prostate gland remain unchanged.

INFECTIONS OF THE URINARY TRACT

Goldstein⁷⁵ reviewed the pathogenicity of three common gram-positive cocci in the urinary tract, namely, *Staph aureus*, *Micrococcus* and *Streptococcus faecalis*. These bacteria were obtained in pure culture from the urine of patients and were then subcultured. Young male rabbits were used for the study. The animal was first catheterized, the specimen of urine being collected in a sterile test tube of microscopic examination and culture. The solution containing the bacteria was then injected into the lateral vein of the ear of the animal. Forty-eight or seventy-two hours after injection another catheterized specimen of urine was obtained in a sterile test tube for microscopic examination and culture. At necropsy, specimens of urine for culture were obtained from the bladder by aspiration through the sealed surface of the bladder and by drawing the urine into a sterile pipet. Complete necropsy was performed on all animals.

Lesions of the kidney were produced in 73 per cent of 11 rabbits given injections of the staphylococcus. The most common lesions observed, in the order named, were abscesses of the papillae, pyelitis and medullary and cortical abscesses. No abnormal elements were found in the urine of 2 of the 3 animals in which renal lesions were absent.

Fourteen animals were given injections of varying amounts of a culture of *Micrococcus*, and in no cases was any renal lesion produced. Likewise, no abnormal elements were found in the urine of any of these animals.

In 37 per cent of the 19 rabbits receiving injections of *Str faecalis* lesions developed in the kidney. Pyelitis, abscess of the medulla, papillary abscesses and cortical abscesses were observed most frequently, in the order named. The lesions produced by *Staph aureus* were far more intense than those caused by *Str faecalis*. Forty-eight hours after injection the urine of 5 rabbits contained pus.

Goldstein suggested on the basis of his observations, that the presence of *Micrococcus* which is so common in vesical urine does not

⁷⁵ Goldstein M. The Pathogenicity of Cocci Isolated from the Urine. Proc Staff Meet Mayo Clin 13: 774-776 (Dec 7) 1938.

necessarily indicate infection in the upper part of the urinary tract, whereas the presence of *Staph aureus* in the urine usually indicates renal infection. The frequency of renal lesions following the intravenous injection of *Sti faecalis* indicates that its presence in the urine is of pathologic significance.

URINARY LITHIASIS

Higgins⁷⁶ stated that diligent postoperative routine is required to prevent the formation of recurrent calculi.

Conservatism in surgical treatment is advisable. Application of the high vitamin A, acid ash or alkaline ash diet is of value in the prevention of recurrent calculi and in the prevention of the formation of calculi in patients who have orthopedic conditions and in those who pass calculi at frequent intervals but who do not have renal calculi. The high vitamin A, acid ash or alkaline ash diet is also of value in the solution of calculi in a selected group of patients.

Complete bacteriologic study of the organisms present in many cases of lithiasis is essential in order that proper medication may be prescribed for eradication of the infection.

Close follow-up observation for three years, which is the maximal period of formation of recurrent calculus, is essential.

UROGRAPHY

Moore⁷⁷ stated that the serial pyelographic apparatus, a comparatively simple and inexpensive device, renders possible the utilization of one standard 14 by 17 inch (35.5 by 43.2 cm) film for three pyelograms, or pyelograms in triplicate. These may be made rapidly, registering different phases of the phenomena of motility, or with definite intervals between exposures for studying the emptying time. It has been found of particular value in examination of the ureter with special reference to strictures, kinks, atony and shadows suspected of being of calculous origin. Serial pyelograms have been found of value in determining the site and nature of the obstruction in hydronephrosis, in the diagnosis of renal mobility, intrapelvic filling defects and perirenal inflammatory conditions and the identification of shadows in the renal region. Economy of films made possible by this device is worthy of mention, especially in excretory urography and in obtaining delayed exposures during retrograde pyelography.

⁷⁶ Higgins, C. C. Urinary Lithiasis. Collective Review, *Surg. Gynec. & Obst.* **68** 392-405 (April) 1939.

⁷⁷ Moore, T. D. Pyelograms in Triplicate. Advantages of the Method. *J. Urol.* **41** 177-187 (Feb.) 1939.

Maintz, Meese and Wullenweber⁷⁸ discussed ureteral peristalsis. They drew attention to a number of observations that can be obtained by roentgenkymographic studies of ureteral peristalsis. They found retroperistalsis in a number of cases, the condition occurred in 2 cases of coral stone of the renal pelvis, in 1 case of pyeloureteritis and in a fourth case in which there was a noninfected fistula of the ureter. One part of the ureter showed normal peristaltic and the other retroperistaltic waves.

MULTIPLE PRIMARY TUMORS

Kretschmer⁷⁹ gave detailed reports of 5 cases of multiple primary malignant growths. In 3 cases the multiple tumors were situated in the urogenital tract, and in 1 case one of the tumors was situated in the prostate gland and the other on the ear. In the first case there were three primary malignant tumors. Studies indicate that the figures regarding the occurrence of these tumors show a greater incidence in the United States than in Europe. Cases of this type are probably more common than has been the impression heretofore.

SULFANILAMIDE THERAPY

In a recent study of the effects of sulfanilamide, Marshall⁸⁰ showed that the oxygen capacity of the blood was not appreciably lowered by cyanosis, suggesting that methemoglobin or sulfmethemoglobin was not the main cause of cyanosis. These observations indicate that cyanosis does not necessarily demand discontinuance of the drug. Acute hemolytic anemia and agranulocytosis are the serious toxic manifestations of the drug. In a series of dogs it was found that in twenty-four to forty-eight hours after administration more than 90 per cent of the drug was excreted in the urine. The residue so obtained was unchanged sulfanilamide.

Renal excretion of sulfanilamide is about 25 per cent of creatinine clearance. This means that sulfanilamide is eliminated by glomerular filtration in a manner similar to that of urea, but is reabsorbed by the tubules to a greater extent. The fact that its excretion is hastened, or even doubled, by the administration of water is important for two

78 Maintz, M. Meese, J. and Wullenweber, G. Röntgenkymographische Untersuchungen über normale und krankhafte Bewegungsvorgänge an den abführenden Harnwegen. *Ztschr. f. Urol.* **32** 682-690 (Oct.) 1938. Maintz, M. and Meese, J. Röntgenkymographische (urokymographische) Untersuchungen über Retroperistaltik des Harnleiters. *ibid.* **32** 756-763 (Nov.) 1938.

79 Kretschmer, H. L. Multiple Primary Cancers. *Tr. Am. A. Genito-Urin. Surgeons* **31** 161-188, 1938.

80 Marshall, E. K. Jr. Pharmacology of Sulfanilamide. *J. Urol.* **41** 8-13 (Jan.) 1939.

reasons. First, if the urologist wants to keep sulfanilamide in the patient's body, he does not have to force fluids, second, if toxic symptoms develop, forcing fluids hastens elimination of the sulfanilamide.

The proper clinical use of sulfanilamide must, in the opinion of Long, Bliss and Feinstein,⁸¹ be based on knowledge of the factors concerned in its absorption and distribution in the body. They expressed the belief that values for sulfanilamide of from 10 to 15 mg per hundred cubic centimeters of blood are favorable for the control of severe infections. Lower values (from 5 to 10 mg) are satisfactory for the control of mild or moderately severe infections. The maintenance of a constant value is dependent on the dose for the entire twenty-four hour period. Because of the possible toxic manifestations of the drug, patients receiving sulfanilamide should, whenever possible, be hospitalized. This supervision should consist of careful clinical observations, frequent and regular recordings of temperature, a daily determination of hemoglobin and a daily total leukocyte count.

Alyea, Daniel and Yates⁸² stated that the excretion curves for sulfanilamide and its two derivatives practically parallel the blood concentration curves. Patients with poor renal function have a higher concentration in the blood and lower excretion in the urine with the usual dosage. In unilateral renal disease the differential curves for sulfanilamide excretion follow their corresponding differential phthalein curves.

Cook⁸³ stated that the relative frequency of toxic symptoms following the administration of sulfanilamide suggests the need of an equally effective compound of less toxicity. Reports that the toxicity of neoprontosil (the disodium salt of 4-sulfamidophenyl-2"-azo-7'-acetylaminol'-hydroxynaphthalene-3',6'-disulfonic acid) is less than that of sulfanilamide, and that a smaller amount of sulfanilamide appears in the blood and urine after the administration of neoprontosil seem to indicate that the dose of this drug should be equal to, or greater than, that of sulfanilamide.

Cook reported on approximately 100 patients who received neoprontosil for infection in the urinary tract. The usual dose was 60 grams (about 4 Gm) daily, in divided doses. As is the case with other urinary antiseptics, neoprontosil is most efficacious when it is used in cases of

81 Long, P. H., Bliss, E., and Feinstein, W. H. Mode of Action, Clinical Use, and Toxic Manifestations of Sulfanilamide, *J. A. M. A.* **112** 115-121 (Jan 14) 1939.

82 Alyea, E. P., Daniel, W. E., and Yates, A. Sulfanilamide and Derivative amide Concentrations in the Blood and Urine, *J. Urol.* **41** 14-30 (Jan) 1939.

83 Cook, E. N. The Use of Neoprontosil in Infections of the Urinary Tract. *Proc. Staff Meet., Mayo Clin.* **14** 39-41 (Jan 18) 1939.

simple infection of the urinary tract caused by the usual gram-negative bacilli, the beta-hemolytic streptococci or some of the micrococci. It is of little or no value in treating infections caused by the staphylococcus or *Str. faecalis*. Complicating lesions, such as stone, tumor or cicatricial deformity in the pelvis or calices of the kidneys, will inhibit the action of neoprontosil, and sterilization of the urine will be increasingly more difficult.

Cook concluded, on the basis of data in 100 cases reviewed, that neoprontosil is equally as efficacious as sulfanilamide, however a dose somewhat larger than the one for sulfanilamide is necessary, and treatment must often be more prolonged when neoprontosil than when sulfanilamide is used.

Only 3 patients in this series were unable to take the drug, approximately 10 per cent complained of nausea while receiving neoprontosil. Three patients, all of advanced age, had cyanosis of a mild degree after three or four days of administration of the drug. Cook expressed belief that the actual toxicity of neoprontosil is low, since in this series of cases the drug was administered to many persons who had a definite intolerance for sulfanilamide. Neoprontosil has been especially useful for acutely ill patients or those who require a prolonged period of treatment.

Vest, Hill and Colston⁸⁴ concluded that sulfanilamide has a directly bactericidal action on urine. The greatest reduction in infection occurs within the first eight hours of ingestion, after which sterilization is not complete an increase may occur. The direct action of sulfanilamide in urine increases with the dose of the drug, the action varies inversely with the number of organisms present. Clinically, infections with a single organism are more readily sterilized than mixed infections.

Farrell⁸⁵ devised a relatively simple operation on the dog by means of which prostatic secretion can be obtained in a pure form, uncontaminated by blood, urine or spermatic fluid. In this way, he attempted evaluation of the bactericidal action of drugs when such drugs are taken into the prostate gland. By giving the dogs sulfanilamide by mouth he has been able to demonstrate the presence of sulfanilamide in prostatic secretion in sufficient concentration to prevent the growth of staphylococcus and colon bacilli in vitro. The drug contained in the prostatic secretion does not decrease the motility or longevity of the sperm.

Summerfeldt and Mitchell⁸⁶ reported on the treatment with sulfanilamide of urinary infections in children. They stated that children

⁸⁴ Vest S. A., Hill J. H. and Colston J. A. C. Experimental and Clinical Observations on Sulfanilamide in Urinary Infections, *J. Urol.* **41** 31-43 (Jan) 1939.

⁸⁵ Farrell J. I. The Treatment of Gonococcal Infections with Sulfanilamide, *J. Urol.* **41** 44-50 (Jan) 1939.

⁸⁶ Summerfeldt P. and Mitchell D. R. Treatment of Urinary Infections in Children with Sulfanilamide. *J. Urol.* **41** 59-63 (Jan) 1939.

tolerate sulfanilamide better than adults. After a single dose of 10 grains (0.65 Gm) the concentration of the drug in the blood reaches 2 to 3 mg per hundred cubic centimeters in from one to two hours. The drug is excreted rapidly, with the result that the concentration in the blood decreases to below 1 mg per hundred cubic centimeters within about four hours. Complications and toxic reactions are uncommon among children. In a group of 40 children, only 1 patient could not tolerate the drug. The conclusions of Summerfeldt and Mitchell are that 75 per cent of urinary infections in children respond curatively to sulfanilamide therapy. The higher percentage of cures in this group may be due to the fact that in most children the infective organisms are pure *B. coli*.

Herrold and Palmer⁸⁷ stated that a subclinical or carrier state has been found to exist in a substantial percentage of patients after the discontinuance of sulfanilamide. Clinical results tabulated as satisfactory, partially satisfactory and unsatisfactory were obtained for equal numbers of patients. The authors stated that a dose of 80 grains (about 5 Gm) daily should be administered only to hospitalized patients. For ambulatory patients the dose should be contingent on clinical and laboratory observations, with a maximum of 60 grains (about 4 Gm) a day.

Crenshaw and Cook⁸⁸ discussed the limitations, dangers and failures of sulfanilamide in the treatment of infections of the urinary tract. They found the use of sulfanilamide attended by many of the limitations that apply to employment of the ketogenic diet and mandelic acid. They expressed belief that the ketogenic diet and, particularly, mandelic acid have proved to be of the greatest value in the treatment of uncomplicated bacilluria and that mandelic acid is still the drug of choice in such cases, in which its use is attended by much less reaction and the results are just as satisfactory as those obtained by sulfanilamide. Sulfanilamide, however, they considered to be much more efficacious for patients having urinary infections associated with clinical deformity of the renal pelvis and calices, with obstruction caused by stone, tumor, congenital deformity or hyperplasia of the prostate gland, or with marked urethritis and prostatitis. The authors stated that sulfanilamide prevents recurrence of infection of the urinary tract from associated chronic prostatitis more efficiently than any other drug as yet available. Infections of the urinary tract caused by such bacilli as *Escherichia coli*, *Aerobacter aerogenes*,

87 Herrold, R. D., and Palmer, E. The Influence of Sulfanilamide on Gonococci and Gonococcal Infections, *Am J Syph, Gonorr & Ven Dis* 22:70-711 (Nov) 1938.

88 Crenshaw, J. L., and Cook, E. N. Limitations, Dangers and Failures of Sulfanilamide in the Treatment of Urinary Tract Infections, *J Urol* 41:64 (Jan) 1939.

Salmonella Shigella and Pseudomonas respond well to sulfanilamide therapy. Experimentally the drug is somewhat more effective when the p_H of the urine is between 7 and 7.5. The efficacy of sulfanilamide in eradicating *Str. faecalis* and staphylococci from the urinary tract is slight. Crenshaw and Cook expressed belief that the important sign of intolerance for drugs is cyanosis and that cyanosis is the warning sign of impending methemoglobinemia or sulfmethemoglobinemia. Approximately 2,000 patients having urologic lesions were treated with sulfanilamide at the Mayo Clinic. In only 3 cases was hospitalization necessary because of a patient's reaction to the drug. Dermal reactions to sulfanilamide are of two types: the one localized to the exposed parts and the other distributed over the entire surface of the body.

The standard dose used by Crenshaw and Cook in cases of non-gonorrheal infections was 40 grains (about 2.6 Gm.) daily, and they rarely exceeded this amount. Their routine dose in cases of gonorrheal infections was 60 grains (about 4 Gm.) daily for three or four days, followed by 40 grains daily for seven days.

Wood⁸⁹ studied 21 cases of acute anemia associated with the administration of sulfanilamide, in a series of 522 patients treated with the drug. The incidence was higher among children than among adults. No definite predisposing factors were noted in an analysis of the 21 cases.

The earliest signs of the anemia appeared between twenty-four and seventy-two hours after the onset of treatment. The maximal anemia occurred usually on the fifth day, and in no case did it occur before the third or after the seventh day.

The anemia has been shown conclusively to be associated with acute hemolysis, but the pathogenesis is at present not known.

Four of 5 patients who had suffered from acute anemia when they were first treated with sulfanilamide suffered recurrences when a second course of the drug was given.

The anemia is treated by the immediate withdrawal of sulfanilamide, the forcing of fluids and transfusions of blood. No deaths have been reported.

It is important that the concentration of hemoglobin be watched carefully during the first week of sulfanilamide therapy.

Ballenger⁹⁰ expressed the opinion that the administration of sulfanilamide decidedly lessened vesical discomfort following transurethral resection. It was not effective, however, in clearing the urine within the first month or so after these operations, but proved to be almost uniformly good in reducing the average infection persisting several

⁸⁹ Wood, W. B. Jr. Anemia During Sulfanilamide Therapy, *J. A. M. A.* 111:1916-1919 (Nov. 19) 1938.

⁹⁰ Ballenger, E. G., in discussion on Crenshaw and Cook.⁸⁸

months or longer after resection. It also seemed to lessen postoperative hemorrhage, probably by controlling infection.

Patients having pyelitis responded well, and usually directly in proportion to the associated relief from ureteral obstruction and the freedom from calculi. The same statement holds true for patients having cystitis.

In the routine treatment with sulfanilamide of 275 patients having well established gonorrhea, the most notable facts, in addition to the not infrequently startling responses, were relief of pain and scarcity of complications, such as prostatitis and epididymitis.

For 105 patients having gonorrhea, recently acquired, sulfanilamide was used in conjunction with mild protein silver. This was employed by sealing 1.5 cc. of a 5 per cent solution of mild protein silver in the anterior portion of the urethra for four hours, once a day, for four days. Eighty grain (about 5 Gm.) doses of sulfanilamide were administered on the first two days, then reduced to 60 grains (about 4 Gm.) for the next two days. Usually the drug was then discontinued, or was discontinued within a week, since it was desirable to know at once the result obtained and whether further treatment was needed. In this group prompt cure, requiring no additional treatment, resulted for 101 of the 105 patients, who received the treatment within forty-eight hours after the discharge had appeared. By no other plan of treatment was the use of sulfanilamide so promptly effective.

The most satisfactory results in the treatment of resistant infections were gained by the combination of sulfanilamide and artificially induced fever. If there were no focal regions of infection, or "dead spaces," or if these were eliminated by the extra application of heat or by other means, three or four fever treatments were usually sufficient, if the oral temperature was maintained at about 104 F (40 C) for four hours.

Garvin⁹¹ summarized the complications following the administration of sulfanilamide. He stated that symptoms of mild toxicity referable to sulfanilamide, such as malaise, lassitude, weakness, headache, dizziness, anorexia, nausea, slightly lowered carbon dioxide-combining power and slight to moderate cyanosis or dyspnea, need not cause concern.

Moderately severe symptoms of toxicity, such as deep cyanosis, marked dyspnea, distinctly lowered carbon dioxide-combining power, severe vomiting, diarrhea, abdominal pain, itching of the skin and slowly developing anemia indicate the need for vigilance, and possibly for reduction of the dose.

Symptoms of severe toxicity, such as fever, dermatitis, acute hemolytic anemia, leukopenia, psychosis or jaundice, demand immediate discontinuance of use of the drug.

⁹¹ Garvin, C. F. Complications Following the Administration of Sulfanilamide, *J. A. M. A.* **113** 288-290 (July 22) 1939.

To avoid toxic manifestations, the patient should be observed closely, the blood examined daily and the use of sulfates and other drugs avoided, and sulfanilamide should not be used for patients who have anemia, leukopenia or hepatic damage.

The treatment of these toxic manifestations consists of the immediate withdrawal of the drug, rest in bed, forcing of fluids, transfusions of blood and such miscellaneous measures as are indicated, that is, administration of extract of yellow bone marrow, pentnucleotide, liver extract iron, oxygen, methylthionine chloride (methylene blue), sodium lactate, Ringer's solution, dextrose and insulin.

Notices

A NEW FEATURE OF THE ARCHIVES FOR 1940

Plans are being made for the publication of symposiums on various subjects in the ARCHIVES during 1940. Symposiums on peripheral vascular lesions, preoperative and postoperative care of patients, treatment of compound fractures and surgical diseases of the esophagus are at present being developed.

In Memoriam

WILLIAM J MAYO, M D
1861-1939

CHARLES H MAYO M D
1865-1939

After a brief separation death reunited on the morning of July 28 1939 two brothers, William and Charles Mayo, whose lives were a sustained union of ideals work and affection A rare and wonderful example!

The two brothers were the branch of a paternal tree from which they derived the good will, probity, energy, stability and sound judgment for which they will always be remembered

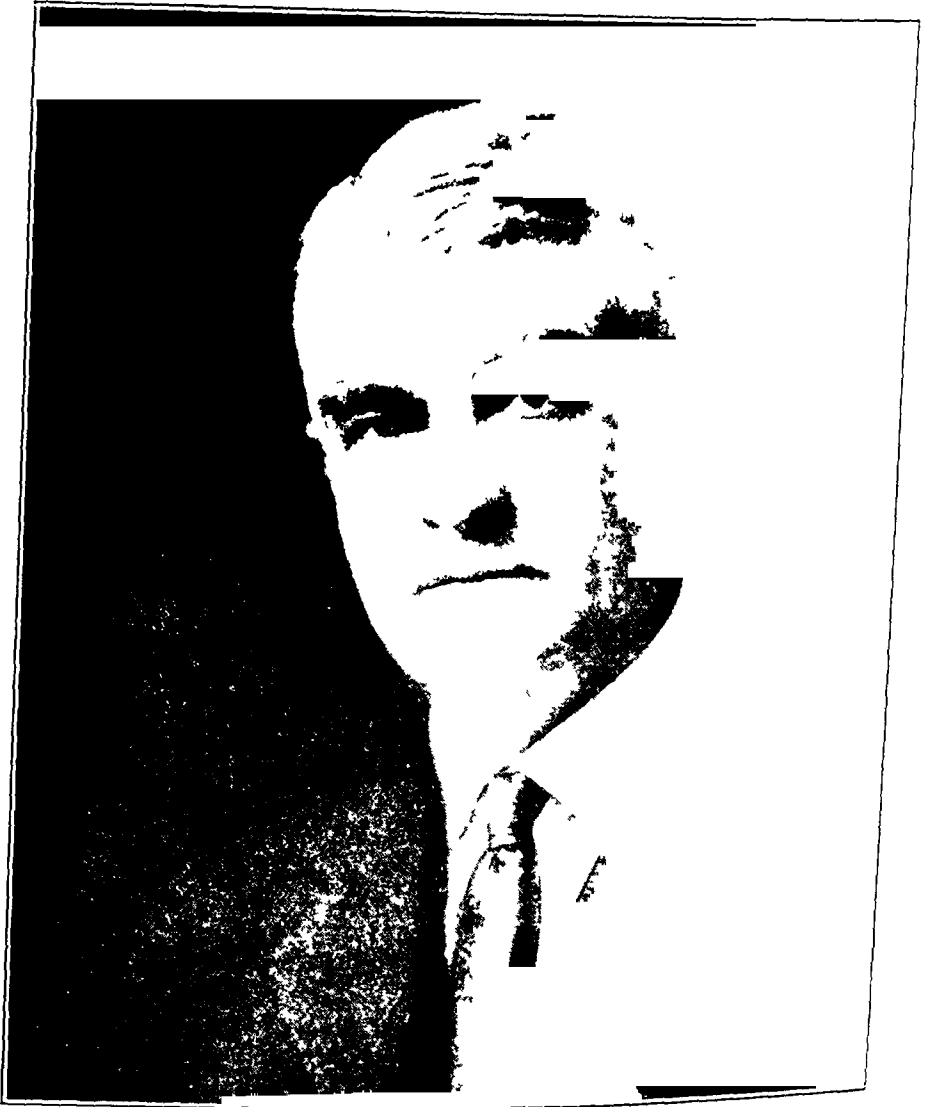
I had the good fortune to meet them in 1905, and when writing to William in the thirtieth year of our acquaintance I referred to the period as "heroic," because the activity of the clinic, already large and developing rapidly in the field of surgery, was dominated by the two brothers almost alone Judd, who completed the trio also an able and a judicious operator was initiating at that time his independent work The operating rooms of the two brothers were separated by the sterilizing room, and they were always at the disposal of one another for consultation For example in the performance of abdominoperineal resection of the rectum, when Dr William completed the abdominal portion of the work, Dr Charles began the perineal

Both were able and were eminently gifted with great clinical as well as practical sense, the fruit of a medical education which was begun in their youth by their paternal guide Charles appeared to be probably a little more dextrous and skilful of hand and rich in resources, while William was more thoughtful and turned more to the study of general problems Of the two brothers one is able to say that one was the strategist or the head, and the other the collaborator Both were inspired by the vision of an ideal clinic which already was taking form for its future development, and they contributed assiduous work and a judicious practice

I do not know which one of the two admired the other one most, but only one who has lived with them intimately as I did and witnessed the indissolubility of their spirits, unassuming but free of the commonplace, can know how much they were united in affection

This is a translation of "In Memoria di William e Charles Mayo," by Raffaele Pastanelli which was privately printed in Rome, Italy

I cannot enumerate the contributions that the two brothers made to surgery. They would make a long and interesting volume and can be found in the annual publications of the clinic. For my part, I think of the two brothers as teachers and friends—dearest friends who were expecting me in September for our last meeting. I remember their

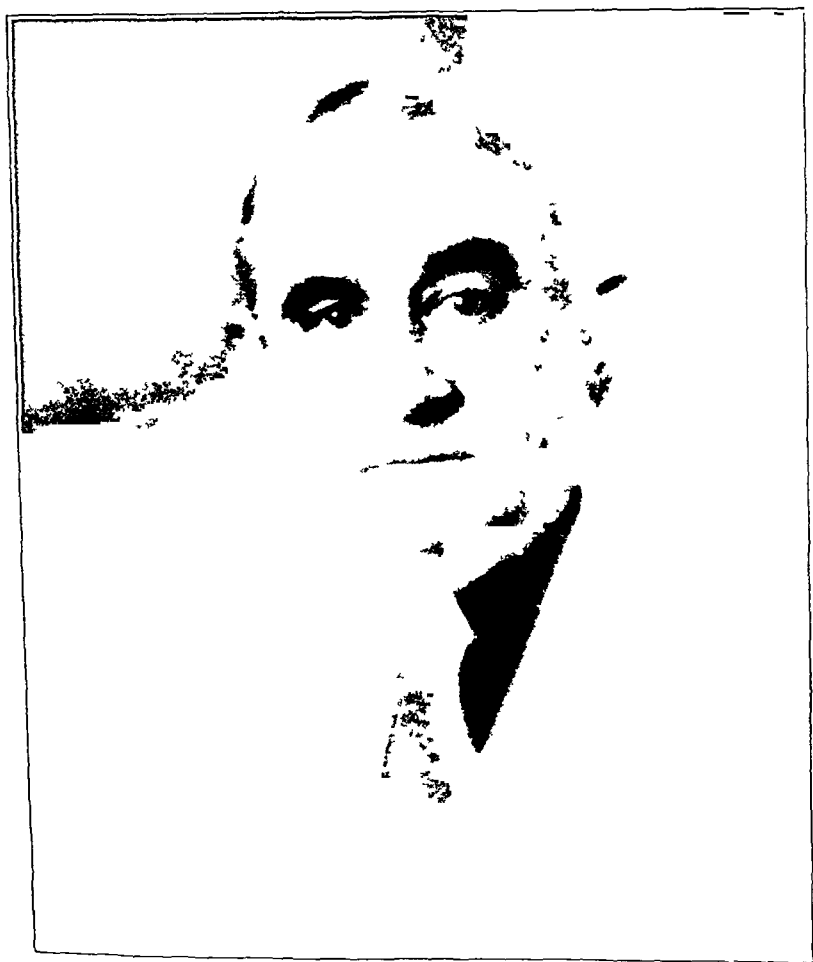


WILLIAM J. MAYO, M.D.
1861-1939

ments as the creators of the Mayo Clinic, a stupendous example of an ideal that shall serve to guide every other clinic, small or large—an ideal of the union of work and study and of perfection and mutual help.

The injustice, and I should even say the iniquity, of the words of a few of the hurried and ungrateful visitors to Rochester who have stated that the clinic is a standardized affair demonstrates an interior mentality

The work does begin punctually at 8 o'clock and proceeds rigorously with silent discipline, but the work is prepared by the study and conscientiousness of physicians, specialists and scientists working together harmoniously as colleagues to give the patients the best treatment briefly and successfully



CHARLES H. MAYO, MD
1865-1939

Those who have not seen or understood this ideal beyond the immense daily work so well performed in the Mayo Clinic, an ideal of superiority, as far as one can be reached have not understood the superior spirit of the two brothers who exerted such an enormous influence on the development of American surgery. They never spared their own time to instruct themselves and to educate their collaborators. The latter went

and were sent wherever progress was being made or wherever anything was to be learned. These factors demonstrate how much the Mayo brothers were enlightened in scientific studies, in instruction and in securing distinguished men gifted in science and in fields of practice.

I remember one evening I saw the clinic building and the hospitals of Rochester from a height. William told me "All this has occurred because of the good will of patients, in spite of ourselves, we not knowing how to stop the stream. But to the sick and to the studious all shall be returned." This they achieved. They allowed themselves and their staff a fixed salary, and anything left over was placed in a community foundation for the perfecting and constant development of study for the cure of the ill. The excess earnings were to be used for the betterment of the clinic and for the expenses of patients who could not afford to pay. Finally, William even gave his home to the physicians. To the two brothers, an unforgettable example to me of men and surgeons, I dedicate these few words, and I should like to say how great my grief is that I can never see them or be able to hear their words again, which were so sincere, modest and pure and full of significance.

RAFFAELE BASTIANELLI

SURGICAL ASPECTS OF ACUTE ABDOMINAL DISEASE IN INFANCY AND IN CHILDHOOD

CHARLES W. McLAUGHLIN, JR., M.D.

AND

HERBERT H. DAVIS, M.D.

OMAHA

Few medical problems offer greater difficulties than early, accurate diagnosis and correct treatment of the acute abdominal diseases of infants and children. Because of the treacherous behavior of these diseases, the general surgeon who observes relatively few of the children suffering from them is at especial disadvantage. The purpose of this paper is to present our surgical experience with a series of patients varying in age from birth to 12 years, together with a review of the recent literature.

It has generally been recognized that surgical treatment of infants and children must differ greatly from surgical treatment of adults. In patients under the age of 12 years the unstable metabolism influences markedly the reaction to acute peritoneal lesions. Requirements of food and fluid are more constant in children than in adults because of growth and its demands on the tissues, temporary interruption of these supplies is detrimental and may in a short time become serious. Rapid and dangerous loss of essential body fluid quickly results from such common symptoms of acute abdominal disease as vomiting and diarrhea. This alteration of the fluid balance, which develops rapidly into acidosis in all acute abdominal emergencies, cannot be too strongly emphasized. Prompt and complete restoration of fluid balance is necessary for successful treatment. The administration of dextrose and saline solution by vein or of saline solution by subcutaneous injection often permits a seemingly hopeless condition to be treated successfully by surgical intervention. In cases of excessive and protracted loss of fluid, we prefer lactate-Ringer solution (as devised by Hartman). In our opinion the subcutaneous use of dextrose even in weak concentrations is never justified, being associated with increased pain and appreciable risk of serious infection in the soft tissues. If dextrose is indicated, venoclysis should be used.

Unlike the great majority of such conditions in adults, acute abdominal emergencies in infants and children cannot be diagnosed from the

history alone. The observer, not the patient, furnishes most of the history, a description of early and prodromal symptoms can rarely be obtained, and all too frequently the condition is far advanced when advice is sought. An evaluation of the physical findings, therefore, is of great importance. Abdominal pain, usually the primary symptom, must be differentiated according to its origin, whether visceral or peritoneal. Edwards¹ listed the principal characteristics of each type, and, though his classification is not absolute, it is of great assistance.

Peritoneal	Visceral
Localized	Diffuse
Constant	Intermittent
Reflex rigidity of abdominal wall muscle	No rigidity of abdominal wall muscle
Elevated temperature	Normal or subnormal temperatures

Visceral pain, extremely common in childhood and usually the most prominent symptom, associated with little or no localizing tenderness, tends to improve promptly with expectant treatment. Stephens² observed that colicky pain is eased by pressure, whereas pain from inflammation is increased by pressure. In infancy, however, visceral pain may be of serious import if accompanied by other definite findings, as in cases of intussusception.

Peritoneal pain must always be considered of serious import, since it is evidence of an inflammatory process within the peritoneal cavity. The examiner's problem is to determine the presence of real localized tenderness with associated muscle guard or rigidity.

It is well recognized that the threshold of the nervous system for pain varies markedly in different persons. As a group, infants and, to a lesser degree, children react to pain differently from the average adult. Apfel³ pointed out that the average child, probably because of underdevelopment of the nervous system, is much less disturbed than is the adult by the pain of acute abdominal disease. Very young children rarely show abdominal rigidity in acute visceral pathologic conditions but do show distention. The infant usually evidences pain by frequent crying out and flexing the thighs on the abdomen. Tenderness can usually be demonstrated if the lesion is inflammatory. In the very young, in the absence of pathologic change in the throat, chest or kidneys, local abdominal tenderness accompanied by nausea and vomiting indicates intraperitoneal inflammatory disease.

1 Edwards, H. C. *Surgical Emergencies in Children*, New York, William Wood & Company, 1936, p. 95. Morley, J., cited by Edwards.

2 Stephens, H. D. *The Acute Abdomen in Infancy and Childhood*. M. J. Australia **1**: 465, 1938.

3 Apfel, H. Significance of Abdominal Pain in Children in Light of Recent Studies, *Arch. Pediat.* **47**: 17, 1930.

Abdominal examination is often difficult because of the child's reaction. Fraser⁴ recommended the use of very light anesthesia for certain children, especially if intussusception is suspected, to facilitate careful palpation and accurate diagnosis. We have not used this method, but it is worthy of consideration. Certainly warm hands and gentleness win the young patient's confidence and aid in obtaining the necessary information.

Acute appendicitis is the one acute abdominal lesion common to all age groups. For all practical purposes the common lesions of adult life with the exception of appendicitis may be excluded, and in their stead a different array of conditions must be considered.

In table 1 reports of nine large series of admissions to children's hospitals for acute conditions of the abdomen are analyzed. This compilation strikingly illustrates the limited number of types of pathologic processes responsible for the disease in the vast majority of cases. Appendicitis, as in adult groups, is the most frequent pathologic lesion, being present in from 40 to 90 per cent of the reported cases. Intussusception is second, followed closely by streptococcic and pneumococcic peritonitis. The rest of the series, less than 10 per cent, shows a wide variety of conditions infrequently encountered. Although the great variety of developmental anomalies observed is worthy of emphasis, such anomalies are omitted because of their relatively small number. Discussion in this paper is limited to differential diagnosis and treatment of the four conditions listed as comprising over 90 per cent of acute abdominal diseases in children.

We are reporting on a series of 89 children under the age of 13 years admitted to the hospital for acute abdominal disease and observed during the last five years. In this series acute appendicitis was present in 62.9 per cent, intussusception in 4.4 per cent and streptococcic and pneumococcic peritonitis in 3.3 per cent. In the remaining 29.4 per cent a wide variety of other acute abdominal conditions occurred.

APPENDICITIS

Age Incidence and Mortality—In all age groups appendicitis is the condition most commonly encountered in such acute cases, constituting from 50 to 90 per cent of all acute conditions of the abdomen requiring operation in children from birth to the age of 13 years. Although it is encountered with increasing frequency after the age of 5 years, it occurs in a sufficient number of younger children (with a distressingly high mortality) to warrant discussion of the subject with regard to both age groups.

⁴ Fraser, J. (a) *Appendicitis in Childhood*. New York: William Wood & Company, 1926, vol. 2, p. 823. (b) *Some Aspects of the Abdominal Emergencies in Childhood*. Edinburgh: M. J. 1922.

TABLE 1—Admissions of Children with Acute Abdominal Disease (Ages 1 to 12 Years)

Author	Year	Total Cases	Acute Appendicitis		Intussusception		Intestinal Obstruction		Congenital Abnormalities		Streptococci or Pneumococci Peritonitis		Tuberculous Peritonitis		Pyloric Stenosis		Miscellaneous	
			Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality
Litchfield, H. R., and Denbo, L. H. Acute Abdominal Conditions in Children, Illinois M. J. 6: 222, 1933	1921	206	124 60.1%	25%	11 5.3%								12 5.8%				39 28%	
Landman ²³	1921	543	223 40.1%	13%	72 13.2%	41%	20 3.6%	50%			16 2.9%	7.5%	49 9%	14%	66 12.1%	9.9%	11 8%	
Beckman ⁸	1925*	330	316 90%	30%							12 3.6%	65%+					2 0.6%	
Cohen ⁶	1927	400	327 82%	4%	22 5.5%	22.7%	35 8.7%				10 2.5%	80%					29 7%	
Horgan and Horgan ¹⁰	1929	319	236 74%	8.4%	13 4%	30.7%	12 3.7%	33.3%	8 2.5%	7.5%			6 1.8%	33.3%	32 10%	2.2%	10 3.1%	30%
Portis, B. Acute Surgical Abdominal Conditions in Children, Illinois M. J. 63: 222, 1933	1933	153	145 92%		6 3.7%	0%					5 3.1%		2 1.2%					
Hudson ¹⁰	1934	1,107	717 65%		90 8.1%		62 5.6%		30 2.7%		29 2.6%				181 16.4%			
Barrington Ward ²⁴	1936	287	42%		37 6%		7.7%				7.7%						8%	
Stephens ²	1938	1,002	769 76.5%	4.4%	144 14.5%	12.5%	67 6.7%	41.8%									2.5%	
McFaulklin and Davis (this paper)	1939	89	56 62.9%	8.9%	4 4.4%	2.5%	2 2.2%	0%			3 3.3%	0%	1 1.1%	0%	13 14.8%	7.5%	10 11%	0%

* All inflammatory lesions

Appendicitis, rare in children under the age of 2 years, occurs in a rapidly increasing proportion of those above this age. Ladd⁵ reported that 34 per cent of 200 patients were under the age of 6 years, Cohen⁶ that 19 per cent of 312 patients were under the age of 5 years. Christopher⁷ observed the condition in 30 children under the age of 5 years, and Beekman⁸ noted that 14 per cent of his 280 patients were in the age group from birth to 6 years. In the last-mentioned age group Ladd⁵ reported a mortality of 19 per cent, Beekman⁸ 25 per cent and Christopher⁷ 30 per cent. In our own series only 3 patients, or 5.3 per cent, were under 6 years of age, all had spreading or general peritonitis when seen and the mortality was 66.6 per cent.

The reasons for these high mortality figures may be considered under two headings: (1) the difficulty of diagnosis and (2) the rapidity of the process, due to anatomic and physiologic factors peculiar to this age group.

Difficulty of Diagnosis—The usual difficulties of diagnosis are increased by the fact that the physical findings are much less distinct than in the older child. Hartshorn⁹ stated that acute abdominal pain and tenderness localized in the region of the appendix in a child should be classified in every instance as appendicitis until the diagnosis is absolutely ruled out by the development of the process or by the presence of a primary focus elsewhere. Christopher⁷ stated that in the group of children under the age of 6 years diagnosis is best made on the following points, in the order given: (1) tenderness in the right lower quadrant, (2) leukocytosis, (3) rigidity in the right lower quadrant, and (4) abdominal pain. The evaluation of pain and tenderness in these children is always difficult, however, and rigidity is usually lacking or occurs late.

Hudson¹⁰ called attention to the fallacy of the old statement that a "child with abdominal disease is said not to sleep or let any one else sleep. Even with findings typical of acute abdominal disease, these patients may go to sleep and have to be awakened for examination. No group of patients becomes ill more quickly, yet with acute abdominal

⁵ Ladd, W. E. The Acute Surgical Abdomen in Children, Pennsylvania M. J. **34** 153, 1930.

⁶ Cohen, M. Acute Surgical Diseases of the Abdomen in Children, Surg., Gynec. & Obst. **45** 595, 1927.

⁷ Christopher, F. Appendicitis in Children Under Five Years of Age. Am. J. Dis. Child. **31** 525 (April) 1926.

⁸ Beekman, F. Acute Inflammatory Diseases of the Abdomen in Children, Arch. Pediat. **2** 782 1925.

⁹ Hartshorn, W. E. Surgical Significance of Abdominal Pain in Children, M. Rec. **93** 96 1918.

¹⁰ Hudson, H. W. Jr. Abdominal Emergencies in Infancy and Childhood, Rhode Island M. J. **17** 18, 1934.

disease the picture is often confusing Hughes^{13b} has wisely stated, "The child is never too sick to be despaired of nor too well to be sure of" All these factors make acute appendical disease treacherous and cause a high mortality in this age group

In children above the age of 5 years appendicitis becomes increasingly common but is somewhat easier to diagnose because the surgeon can obtain some history, however fragmentary, from the patient

Appendicitis in the child proceeds through the same established sequence of symptoms and physical findings as in the adult generalized abdominal pain, nausea and vomiting, tenderness, fever and leukocytosis Without careful and intelligent questioning of the patient or of the parents the history in its correct chronologic order, so important for correct diagnosis, cannot be obtained

Initial abdominal pain, either paraumbilical or epigastric, was the first symptom in from 75 to 90 per cent of a series of reported cases It was followed by nausea and vomiting in from 75 to 95 per cent, with subsequent development of local tenderness over the appendix in a like percentage (table 2) Rigidity, observed in from 75 to 80 per cent of the cases, should never be considered essential to diagnosis, since its presence indicates that the inflammatory process has passed through the visceral peritoneum and involved the parietal peritoneum, a late sign Chills are associated with acute appendicitis in children in approximately 5 per cent of cases, they demand early treatment to prevent involvement of the portal vein or of the liver Diarrhea is occasionally observed, especially if the appendix is in the pelvis Routine rectal examination is valuable in making a diagnosis, for the shallow pelvis of the child permits much more thorough exploration than is possible in the adult

The white blood cell count in cases of appendicitis in children may be of equivocal value One occasionally sees a child with the typical history and physical findings of appendicitis and a normal white cell count, the diagnosis being confirmed at operation A normal white cell count should never be thought to exclude appendicitis if the history and abdominal findings are suggestive The average leukocyte count in our series of cases was 15,000 per cubic millimeter Counts above 20,000 per cubic millimeter are not common in cases of uncomplicated appendicitis

Rapidity of Advance Toward Perforation—Pathologically the process is too often far advanced when the child is first seen A gangrenous or a ruptured appendix with local peritonitis is the rule rather than the exception, and spreading peritonitis is a common finding (table 3) In general, 50 per cent of all patients with acute appendicitis under the age of 13 years require drainage at operation, as do approximately 95 per cent of the group below the age of 5 years In our own series drainage was considered necessary in 32.1 per cent of cases

TABLE 2—*Acute Appendicitis in Infancy and Childhood (Birth to 12 Years) Analysis of Clinical Observations*

Author	Cases	Boys	Girls	Previous Attacks	Associated Infection of Tract	Initial Pain	Nausea and Vomiting	Abdominal Rigidity	Average Temperature	Chills	Distention	Average White Blood Cells
Itchikoff, H. R., and Denbo, J. H. Acute Abdominal Conditions in Child in Illnesses M. J. 41: 222, 1933	116	62%	38%			90%	9%	8%	101.1	6.8%	14%	16,000
Solokoff ¹⁷	61	67%	25%			90%	7.2%	80%+	Variable			17,000
Cohen ⁶	312	42%	15%		8.6%	75%	8%	7.7%+				17,000
Freedman ¹	42			16%	1%				100.4-1			14,200
Hudson ¹⁰	200					99%	92.8%	94.4%				
Hamilton, H. B. Nebraska M. J. 24: 164, 1938	70			3%	52%	7%	75%+	90%	100.2-1			10,000
McLaughlin and Davis (this paper)	76	60%	40%			75%	90%+	9.9%+	100.4-1	6%		14,000

TABLE 3—*Appendicitis in Infancy and Childhood (Birth to 12 Years) Analysis of Pathologic Observations in Relation to Treatment and Mortality*

Author	Year	Cases	Percent age of Admis- sions for Abdominal Disease	Pathologic Process										Per centage Treated by Drainage	Deaths	
				Acute Catarrhal or Sup- purative Condition		Gangrene		Rupture, Abscess		Rupture, Peritonitis		Per- centage Number centage				
				Cases	%	Cases	%	Cases	%	Cases	%					
Litchfield, H. R., and Denbo, L. H. Acute Abdominal Conditions in Chil- dren, Illinois M. J. 6:3 222, 1933	1921	116	60	31	25	11	9	15	12	59	47	59	29	25		
Lanman 33	1921	223	32.3	122	55			65	29.5	36	16.1	45+	29	13		
Beckman 8	1925	316	95										22	7		
Seiger 15	1926	61														
Cohen 6	1927	312	85									59	5	8.2		
Freedman 23	1929	42		24	57			18	43			20	13	4		
Horgan and Horgan 16	1929	236	74	122	51	11	4.6	23	11.6	75	31.7	57	2	4.8		
Reves 17	1934	380										43	20	8.4		
Hudson 10	1934	200	65									60	30	7.89		
Hamilton H. B. Nebraska M. J. - 1:16, 1938	1937	76		47	61			29	39			38	2	2.6		
McClucklin and Davis (this paper)	1939	56	62.9	38	68.9			7	12.5	11	19.6	32.1	5	8.9		

Several anatomic and physiologic reasons account for the rapid progression to perforation and peritonitis in children under the age of 6 years

(a) The cecum lies higher and the appendix is less often retrocecal than in older children, making the chances for general peritonitis greater when perforation occurs ¹¹

(b) The lumen of the appendix is proportionately large, offering material free entrance into the appendix, with the possibility of obstruction

(c) Lymphoid tissue gradually increases in the appendix of the child as the latter grows older, with its susceptibility to infection ¹¹

(d) The virulence of *Bacillus coli communis* in the infant increases with age ¹²

(e) The appendical wall in young children is thin, offering little defense to virulent infection ¹²

(f) The omentum is underdeveloped at this age, giving little protection ¹³

(g) The long mesocecum usually present at this age increases the mobility of the cecum ¹⁴

(h) The child's relatively longer appendix tends to wander and give typical physical findings ¹⁴

Treatment—Treatment consists in making the earliest possible diagnosis and in surgical removal of the appendix, preferably through a muscle-splitting incision. Even when there is reasonable doubt as to the diagnosis it is safer to remove the appendix, for the tragedy of one fatal mistake far outweighs any misgivings one may have in occasionally removing a normal appendix.

Removal of the appendix may not always be feasible in the large group of children who are first seen with a well formed appendical abscess. If at operation an abscess is encountered with the appendix incorporated in its medial wall, simple drainage, we believe, is the indicated procedure, with subsequent removal of the appendix in from six to eight weeks. Only when the appendix, presenting itself readily in the center or on the lateral side of the abscess cavity, can be removed without danger of contaminating the general peritoneal cavity is appendectomy carried out at the first operation.

11 Carson H W Abdominal Pain in Children *Canad M A J* 20 587, 1929

12 Fraser, J Mesothelial Reactions in Childhood, *Brit M J* 2 47, 1931

13 (a) Ponter, C W M Concerning the Great Omentum *M Clin North America* 12 499, 1928 (b) Hughes, B Abdominal Crises in Childhood, *Practitioner* 125 65 1930 Fraser ¹¹

14 Stone J S Differential Diagnosis of Acute Abdominal Conditions in Childhood *Boston M & S J* 189 303 1923 Ladd ⁵

Children who present on admission evidence of spreading peritonitis offer a real problem. In the absence of unmistakable signs of general peritonitis our practice is to proceed immediately with appendectomy and, if necessary, drainage. Two factors influence this course in dealing with children. In the first forty-eight hours of the attack, even when the degree and extent of tenderness and rigidity suggest spreading peritonitis, operation may disclose only a diffusely inflamed or a gangrenous appendix without perforation but with a large quantity of free sterile peritoneal fluid. Appendectomy without drainage results in prompt, uncomplicated recovery, yet clinically it is impossible to determine the exact degree of peritonitis.

The second important factor is that anatomically the child's peritoneal cavity is not well adapted to the delayed (Ochsner) method of treatment, for the reasons previously stated. Seiger¹⁵ and Stephens⁹ expressed agreement with this opinion. Only in certain selected cases, in which there are a high temperature, a fast pulse and diffuse rigidity after an illness of three or more days, is the delayed treatment the method of choice. In such cases the extent of the disease and the general condition of the patient constitute a poor surgical risk, and it is our opinion that surgical drainage is never life saving in cases of established general peritonitis.

Factors in Mortality—The various reported series of children operated on for acute appendicitis and its accompanying complications have shown a mortality ranging from 3 to 15 per cent. The two most important factors in this connection in any series are the age of the patient and the extent of the pathologic process found at operation. In series composed chiefly of young children the mortality is very high, as has been noted. In the entire group from birth to the age of 12 years the mortality varies with the number of patients with perforation of the appendix and with the extent of the peritonitis. Thus, Horgan and Horgan,¹⁶ with a series of 236 children operated on for acute appendicitis, reported no mortality in 122 whose appendixes were not perforated, 9 per cent mortality in 11 whose appendixes were gangrenous, 18.6 per cent mortality in 75 whose appendixes were gangrenous and perforated, and a mortality of 17.8 per cent in 28 whose appendixes had ruptured with abscess formation. In our series of 56 children the mortality was 8.9 per cent. There were no deaths among those with acute appendicitis but no rupture, 1 death (a mortality of

15 Seiger, S. J. Appendicitis in Infancy and Childhood, *Surg., Gynec. & Obst.* **42**: 536, 1926.

16 Horgan, E., and Horgan, J. Acute Surgical Conditions Within the Abdomen Occurring During Infancy and Childhood. Study of Three Hundred and Nineteen Cases, *Arch. Surg.* **18**: 2271 (June) 1929.

14.3 per cent) among those with perforation and localized abscess, and 4 deaths (36.3 per cent) among 11 who had spreading or general peritonitis

The factors which we believe to be chiefly responsible for the high incidence of perforation and its attendant mortality are (1) the difficulty of diagnosis in the early stages of the disease, (2) the rapidity with which the changes progress to perforation and (3) the administration of purgatives by the mother or the physician

The first two factors are well appreciated and require no further comment. The crusade against purgation has, however, just begun. Keyes¹⁷ recently reported a mortality of 17.6 per cent in 193 children with acute appendicitis who had received a laxative prior to admission and a mortality of 2.4 per cent in 42 children with the same disease who had received no purgatives. Until both mothers and physicians have been taught that laxatives have no place in the treatment of acute abdominal disease, management of this problem will continue to show little improvement.

Differential Diagnosis—Smith,¹⁸ in a critical analysis of the observations on 146 children admitted to the hospital with a major complaint of abdominal pain, found that 68 per cent, or approximately two thirds, had acute surgical abdominal disease. In the remaining third the pain was due to a variety of nonsurgical conditions, and it is these which must be excluded by differential diagnosis. Since appendicitis is much the most common acute lesion requiring surgical treatment in this group, the problem often resolves itself into differentiating appendicitis from the more common conditions which do not require operation. In our experience the following diseases have offered the principal difficulties in diagnosis: (1) enterospasm, (2) acute sore throat or infection of the respiratory tract with abdominal pain, (3) mesenteric adenitis, (4) cyclic vomiting with acidosis, (5) pyelitis and cystitis, (6) pneumonia with abdominal pain and (7) abdominal purpura.

1. *Enterospasm*. This is considered by Heiman and Cohen¹⁹ the most frequent cause of abdominal pain between the ages of 4 and 12 years. In the infant it is commonly induced by hunger, tends to recur at the same time each day and is usually controlled by food and atropine. In the older child the picture may be confusing. The three characteristic symptoms are paraumbilical pain, vomiting and constipation. The pain results from spasm of the smooth muscles, comes on

17. Keyes E. L. Deaths from Appendicitis, *Ann Surg* 99:47, 1934.

18. Smith F. H. Diagnosis of the Acute Abdomen in Children, *Virginia M Monthly* 54:271, 1927.

19. Heiman H. and Cohen P. Abdominal Pain in Children Due to Enterospasm, *Arch Pediat* 45:383, 1928.

suddenly, is severe and tends to recur at intervals of several weeks. Examination discloses no local tenderness, muscle guard or rigidity and usually no fever or leukocytosis, but a spastic, cordlike bowel can frequently be palpated. Administration of atropine usually results in prompt recovery.

2 Infection of the respiratory tract. The frequent association of an acute sore throat or infection of the upper respiratory tract with abdominal pain is now well appreciated. The abdominal pain is characteristically paraumbilical and tends to be rather severe but is not accompanied by local tenderness or rigidity. Brennemann²⁰ concluded that this abdominal pain is resultant from swollen abdominal mesenteric glands but warned that associated appendicitis may be present. Subsequently²¹ he has emphasized the great frequency with which acute appendicitis is seen in association with infections of the upper respiratory tract. In 1918 Evans²² published his observations on the association of acute tonsillar infections with appendicitis among students at the University of Wisconsin. He found, over a five year period, active or recent acute tonsillar infection in 86 per cent of 236 patients admitted to the hospital with acute appendicitis. Freedman²³ reported the occurrence of acute appendicitis in 42 children during an epidemic of acute infections of the upper respiratory tract. Undoubtedly infections involving the upper respiratory tract have a special predisposition to invade the appendix, and when this occurs the process advances rapidly to perforation. The important clinical fact is that the two conditions frequently coexist, and the presence of localizing tenderness over the appendix with muscle guard or rigidity, if accompanied by a sore throat, demands extremely prompt attention.

3 Mesenteric adenitis. This condition offers one of the most difficult problems in differential diagnosis. Enlargement of the glands in the mesentery of the terminal portion of the ileum has been thought to be a local manifestation of a general process with the primary infection in the nasopharynx (Adams and Olney²⁴). This is suggested by the frequency with which a recent or an active infection of the throat

20 Brennemann, J. Abdominal Pain of Throat Infections, *Am J Dis Child* **22** 493 (Nov) 1921.

21 Brennemann, J. "Abdominal Pain of Throat Infections in Children" and Appendicitis, *J A M A* **89** 2183 (Dec 24) 1927.

22 Evans, J S. Epidemiology of Acute Appendicitis in Relation to Acute Nasal and Tonsillar Infections, *Wisconsin M J* **17** 91, 1918.

23 Freedman, H J. Forty-Two Cases of Appendicitis in Children Occurring During an Epidemic of Upper Respiratory Tract Infections, *Arch Pediat* **46** 604, 1929.

24 Adams, W E, and Olney, M B. Mesenteric Lymphadenitis and the Acute Abdomen, *Ann Surg* **107** 359, 1938.

is found in association with mesenteric adenitis. Stephens² concluded that the process is due to infection in the lower portion of the ileum and not to either a pharyngeal or an appendical lesion. Clinically the picture is characterized by recurrent bouts of generalized abdominal pain with little tendency to localize. Nausea and vomiting are the rule, and diarrhea is occasionally a feature. Examination discloses diffuse soreness, but localized tenderness is not constant. The enlarged glands can be palpated only occasionally. The temperature is usually somewhat higher than in cases of uncomplicated appendicitis and the white blood cell count ranges from 10,000 to 20,000 per cubic millimeter. Free fluid is not present as a rule but was present in 2 of 5 cases in which we performed exploration. Differentiation of this condition from appendicitis is often impossible, and if there is reasonable doubt it is much wiser to open the abdomen. The appendix may show little or no pathologic change, but firm, enlarged nodes varying in diameter up to 1.5 cm are found distributed through the mesentery of the terminal portion of the ileum. These glands on section show only diffuse hyperplasia, and tuberculous involvement is rare. Southam²⁵ observed that appendectomy usually results in permanent cure of the condition, this has been our observation in 4 instances. After operation the temperature often mounts to 103 or 104 F, but it promptly subsides, and the patient makes an uneventful recovery.

4 Cyclic vomiting with acidosis. This condition is not infrequently mistaken for appendicitis. Severe and persistent vomiting is usually the initial symptom. Abdominal pain develops later, but there is no localizing tenderness or rigidity. The characteristic facies of acidosis is usually present, the cherry-red cheeks and lips and the overanxious countenance. The odor of acetone is readily detected on the breath, and the urine is laden with acetone and diacetic acid. The white blood cell count is usually not elevated. Gibson and Mann²⁶ have suggested that as an aid in diagnosis the patient be given a sufficient amount of water by mouth to produce vomiting. Immediately after emesis the patient tends to relax, the limbs are extended and the abdominal tenderness disappears. The accepted therapeutic measure of giving dextrose by vein is also diagnostic and usually solves the problem, since the child often stops vomiting during administration of the venoclysis and falls asleep. The symptoms then rapidly clear up, and recovery is prompt.

5 Pyelitis and cystitis. Pyelitis and, to a lesser extent, cystitis sometimes closely simulate appendicitis. The higher temperature, the

²⁵ Southam, A. H. The Abdominal Emergencies of Childhood, Practitioner 120:364, 1928.

²⁶ Gibson, J. and Mann, J. Mimicry of the Acute Abdomen in Cases of Cyclic Vomiting in Children, Canad. M. A. J. 17:45, 1928.

atypical onset and the presence of chills, tenderness in the renal regions and in the flanks and pyuria usually make the diagnosis clear, although appendicitis with the appendix lying in an extracecal or a high retrocecal position may simulate pyelitis even to the presence of pyuria. The temporary ureteral block associated with pyelitis may prevent the appearance of pus in the urine. If there is a reasonable doubt as to the correct diagnosis, it is certainly safer to remove the appendix, although the absence of appendical pathologic change and the subsequent development of pyuria may prove the preoperative diagnosis incorrect.

6 **Pneumonia** Pneumonia is one of the most difficult conditions to differentiate from acute appendicitis in children. Adams and Berger²⁷ reported that 17.6 per cent of a series of 145 patients at the Boston City Hospital who were proved to have pneumonia had been admitted to the surgical wards with an initial diagnosis of acute appendicitis. They noted that cough and pain in the chest or vomiting and abdominal pain are not determining symptoms. The child with pneumonia usually looks more ill and shows more systemic reaction, the abdominal rigidity is of a different type, the temperature, the pulse rate and the respiratory rate are usually much higher, and the white blood cell count ranges from 20,000 to 42,000 per cubic millimeter. Careful examination of the chest is always necessary to find the lesion in its early stages, and in case of doubt a flat roentgenogram of the chest may be of great assistance.

7 **Abdominal purpura** The clinical syndrome of Henoch's purpura and abdominal allergy simulating acute abdominal disease has been emphasized by Frazer,²⁸ Bailey²⁹ and Althausen, Deamer and Kerr.³⁰ In children this condition, characterized by petechial or massive hemorrhage beneath the peritoneum of the bowel or its mesentery, may simulate acute disease of the appendix or intussusception.

Althausen and his associates³⁰ suggested the following points in differential diagnosis, favoring purpura: (a) a family history of allergy or urticaria, (b) a personal history of allergic disorders or sensitivity, (c) eosinophilia and (d) demonstrable cutaneous sensitivity.

Unfortunately, cutaneous manifestations often appear late, and without a suggestive history careful search may not be made for petechiae.

27 Adams, F. D., and Berger, B. J. Differential Diagnosis of Lobar Pneumonia and Appendicitis in Children, *J. A. M. A.* **79**: 1809 (Nov. 25) 1922.

28 Frazer, I. Purpura Simulating the Acute Abdomen, *Lancet* **2**: 525 1930.

29 Bailey, H. Purpura as an Acute Abdominal Emergency, *Brit. J. Surg.* **18**: 234, 1930.

30 Althausen, T. L., Deamer, W. C., and Kerr, W. J. The Intestinal Abdomen, Henoch's Purpura and Abdominal Allergy, *Ann. Surg.* **106**: 242 1937.

The application of a tourniquet to an arm for three minutes may be useful in demonstrating multiple petechial hemorrhages below the site of application

Even if one realizes that this disorder or a similar abnormality is present the clinical picture may indicate surgical intervention. We recently observed a 6 year old boy known to have hemophilia who was admitted to the hospital with a history and physical findings typical of appendicitis. Operation carried out because of definite physical findings, disclosed a large retroperitoneal hemorrhage with bleeding into the mesocecum. Recovery was slow but without serious complications, although several transfusions were necessary to control the tendency to bleed.

In the differential diagnosis of appendicitis, abdominal pain due to inflammation of Meckel's diverticulum must be considered, but this requires prompt operation and is not to be grouped with the previously discussed seven causes of abdominal pain in infancy and childhood which do not require surgical intervention. This diverticulum has a low incidence, is congenital and becomes of clinical interest only when it contributes to the development of intussusception or to acute intestinal obstruction, becomes acutely inflamed or causes peptic ulcer with intestinal hemorrhage.

Although Meckel's diverticulum persists in approximately 2 per cent of all persons, complications attributable to it are relatively few. Its association with intussusception has been observed in from 4 to 8 per cent of the reported series.³¹ Collins³² collected 11 cases of Meckel's diverticulum from among 500,000 new admissions to the Los Angeles General Hospital. We have observed 1 case in our series of 89 admissions for acute abdominal disease requiring operation in children under the age of 12. The patient, a boy 6 years of age, presented findings typical of acute appendicitis, although the point of maximum tenderness was slightly more medial than is usual. Just before operation was undertaken he passed some rather bright blood by rectum, which suggested the possibility of Meckel's diverticulum. The appendix was normal, but an inflamed diverticulum was removed from the terminal portion of the ileum. Examination of the specimen showed it to contain in its lining mucosa typical gastric tissue with a definite peptic ulcer.

Cases of Meckel's diverticulum in which there is no bleeding but in which signs of an acute abdominal disorder develop are almost

31 Wade, R. B. Some Abdominal Conditions in Children, M. J. Australia 28 1924 Stephens & Ladd.

32 Collins D. C. Acute Abdomen Caused by Meckel's Diverticulum, Canada M. A. J. 37 564, 1937.

invariably mistaken for instances of appendicitis. In none of Collins' ³² 11 cases was the correct diagnosis made before operation or postmortem examination.

The frequent presence of gastric or pancreatic mucosa within the diverticulum, with ulceration and intestinal hemorrhage, should make one suspect the presence of this condition in any child who passes bloody stools in the absence of signs and symptoms suggesting intussusception or Henoch's purpura.

INTUSSUSCEPTION

Intussusception is the second most frequently encountered cause of an acute surgical condition of the abdomen in infancy and childhood. Although described by Hippocrates, it is still too often considered a rare pathologic entity.

Incidence—According to the reported series (table 1) intussusception is the most common acute lesion requiring surgical treatment in children under the age of 2 years, and comprises from 4 to 8 per cent of all acute abdominal conditions from birth to the age of 12 years. In our own series of cases intussusception was responsible for 4.4 per cent of admissions for acute abdominal disease. Intussusception accounts for 60 to 75 per cent of the admissions for acute intestinal obstruction in infants and children ³³. Since this lesion develops most frequently in children between the ages of 6 and 18 months, a period when other acute inflammatory lesions are relatively infrequent, its importance is further emphasized.

Approximately 65 per cent of intussusceptions occur in boys. The patients are usually well developed and well nourished babies, previously in good health, who have had better than average care.

It is interesting to note that in certain sections of the world, chiefly Australia, very large numbers of cases are reported. Barrington-Ward ³⁴ reported intussusception in 37.6 per cent of admissions to the Great Ormond Street Hospital in London, England, during the past five years. This frequency must not be considered a true index, however, for through established custom patients with certain types of conditions are usually sent to specific hospitals.

Causes—Many etiologic factors have been observed and suggested for intussusception (table 4). The presence along the intestinal tract of some pathologic exciting lesion such as Meckel's diverticulum, a

³³ Lanman, T. H. *The Surgical Abdomen in Children*, Boston M. & S. J. 185, 489, 1921. Cohen ⁶

³⁴ Barrington-Ward, L. E. *Diagnosis and Treatment of Acute Abdominal Conditions in Children*, Tr. Med.-Chir. Soc. Edinburgh, 1935-1936, p. 25, in *Idem*, Edinburgh M. J., March 1936.

TABLE 1.—Intussusception in Infancy

Author	City	Year	Cases 1900-1920 collected	Boys Girls	Mortality (and Deaths)	Bleeding Stools	Palpable Masses	Routine				Per centage Mortality	Effect of Delay on Mortality
								Open Incision	Re- sec- tion	Colo- tomy	Not Stated		
Hess, J. H. Intussuscep- tion in Infancy and Child- hood. Arch. Pediatr. 22: 3 6, 1905	Chicago	1907	114 14 yr			94%		151 (65) re- duced	549 (139) re- duced	109 (35) cov	176 (0) cov	50.2	
Conlin	Sydney, Australia	1907	114 14 yr			94%		133 (14) re- duced	124 (After 14 re- operation)	8 (cov)	0 (re- duced)	73.2	Fatalities av 53 hr
Romalis ¹⁰	London	1918	374	8	3								
Richfield H. R. and Den- bo, J. H. Acute Abdom- inal Conditions in Chil- dren. Illinois M J 61: 222, 1923	Washington D C	1921	11										
Fineman ¹¹	Boston	1921	72										87% fatalities over 24 hr
Farmer ¹²	Edinburgh	1922	700 (9 yr)	61%	37%								
Harper W J. Acute In- tussusception. Boston M J 83: 148, 700, 1922	Boston	1922	112										
Wilde ¹³	Sydney Australia	1924	519 13 yr	297	147								
Colton ¹⁴	New York	1927	22 (15 yr)	15	7								
Carson ¹⁵	London	1929	17										
Horkan and Horkan ¹⁶	Washington D C	1929	13 4 yr										
Todd ¹⁷	Boston	1930	273										
Bulley ¹⁸	Birmingham England	1930	9 collected										
Miller, J. M. Abdominal emergencies in Infancy and Childhood. Illinois M J 63: 509, 1933	Chicago	1933	20										
Portis B. Acute Surgical Abdominal Conditions in Children. Illinois M J 63: 223, 1933	Chicago	1933	6										
Hudson ¹⁹	Boston	1934	372	61%	97%								
Barrington Ward ²⁰	London	1936	88	65%									
McLaughlin and Davis (this paper)	Omaha	1939	4	50%									

polyp or a new growth has been suggested as the cause by Romanis,³⁵ Ladd⁵ and Hudson¹⁰. They reported the presence of such factors in from 4 to 8 per cent of their series. Alteration in diet with hyperperistalsis and diarrhea resulting in irritation of the lower part of the ileum has been suggested as an etiologic factor, since the patients are usually of the age at which a rather general diet is instituted. Wade³¹ concluded that inflamed lymph tissue in the lower part of the ileum, acting as a polyp, is usually present. Fraser^{4b} stated that some defect in the structural arrangement of the splanchnic nervous system is a likely cause, and Treves as well as Clubbe³⁶ suggested that irregular action of the intestinal musculature with spasm of the circular coat may produce invagination. Clubbe³⁶ has suggested the abnormal motility of the colon, due to its persistent mesentery, as a predisposing cause. Finally, Power, cited by Clubbe,³⁶ has called attention to the disproportionate growth of the colon and the ileum during infancy, both being approximately the same size at birth. In 2 of our cases a congenital peritoneal band crossing the cecum was felt to be the cause of intussusception.

Types—Intussusception has been described as the "catching up of one piece of bowel within another piece." For practical purposes three types should be considered:

- 1 An enteric type, distinctly unusual and involving only the small bowel.

- 2 A colic type, involving only the colon. It is not frequent in children, it is occasionally encountered in the sigmoid colon in older patients.

- 3 An enterocolic type, involving the terminal part of the ileum, the cecum and the colon.

The last form is much the most common one in infancy and childhood, beginning in the terminal 6 inches (13 cm.) of the ileum and from there proceeding to the cecum and the distal portion of the colon. As it advances, the mesentery of the terminal portion of the ileum is carried with it, the process resulting in constriction of the invaginated part, edema, mucosal bleeding and finally necrosis.

In the effort to expel the abnormal bolus within the bowel the intussusceptum is pushed farther and farther along the colon until it may become palpable by rectum or may protrude through the anus. The excess of mucus within the lumen of the bowel becomes mixed with blood from the engorged mucosa and when passed by rectum is one of the diagnostic features of the condition. This phenomenon appears

35 Romanis, W. H. C. *The Abdominal Emergencies of Childhood*. Practitioner **120** 364, 1928.

36 Clubbe, C. P. B. *The Diagnosis and Treatment of Intussusception*. Edinburgh, Y. J. Pentland, 1907.

in practically all cases in from six to twelve hours and was observed in each of our 4 cases within seven hours after the onset of symptoms.

Prior to the days of operative intervention in such cases an occasional recovery was reported after the sloughing away of the entire intussusceptum with reestablishment of intestinal continuity by plastic adhesions at the site of invagination. This occurrence was distinctly uncommon, however, and occurred in less than 3 per cent of cases. When the condition is untreated death usually results in a few days from acute intestinal obstruction with associated toxemia.

Symptoms—One rarely sees a patient with acute intussusception during the first moments of illness, but the story which may be obtained from the mother or nurse is so typical that there can be little doubt as to the condition. A previously well baby suddenly screams and draws up its legs as if in agony. In a few moments the screaming ceases, and the infant appears to be in shock. The face is pale and beaded with perspiration, the lips are pinched and slightly blue and the whole countenance indicates that something serious has happened. After a variable period, ranging from a few moments to several hours, the child's color returns and the symptoms of shock disappear. Recurrent attacks of the initial severe pain are not the rule, but at intervals the child whimpers or cries briefly as the intussusceptum is forced along the colon by intestinal peristalsis. Vomiting usually does not occur until late in the disease. In a period varying from six to twelve hours bloody mucus or currant jelly-like material is passed by bowel.

Abdominal distention, tenderness and muscle spasm are late features. During the first twenty-four hours the abdomen is usually flat or scaphoid. Palpation frequently discloses a peculiar emptiness of the entire right side of the abdominal cavity (Dance's sign), resulting from migration of the cecum and ascending colon with the advancing intussusceptum. The mass is usually palpable in the right upper quadrant of the abdomen, along the line of the ascending colon or above the umbilicus, but it may appear anywhere along the course of the colon. The tumor tends to be sausage shaped and several inches in length, but it may be felt as a small spherical mass which becomes more prominent during straining. Inability to palpate the tumor does not exclude an intussusception, since the large liver of a small child may completely cover the mass for a time in its progression through the colon. Rectal examination often first discloses the presence of bloody mucus and should never be omitted. A rectal mass can rarely be palpated under twenty-four hours, this finding therefore, is of prognostic importance rather than of aid in diagnosis. As in any case of acute intestinal obstruction the temperature and the white blood cell count are of little value in making a diagnosis in the early stages.

Differential Diagnosis—Four conditions confused with intussusception in differential diagnosis will be briefly considered

1 Acute appendicitis As has been noted, this condition is uncommon under the age of 2 years, and its onset is neither as sudden nor as dramatic as that of intussusception Vomiting is usually an early symptom, with associated tenderness, rigidity and distention

2 Acute enterocolitis This condition rarely begins as suddenly as does intussusception The bowel movements are usually excessive Abdominal pain and passage of excessive amounts of mucus and later of blood are common to the two conditions, but in the presence of enterocolitis fecal matter continues to be passed, which is never true of intussusception Neither an abdominal mass nor intestinal obstruction develops in the former condition Occasionally acute enterocolitis with its associated hyperperistalsis results in intussusception

3 Rectal prolapse The inability to introduce the finger into the rectum beside the protruding mass, in a simple rectal examination, excludes intussusception

4 Abdominal (Henoch's) purpura This condition may simulate intussusception in almost every detail, even to the presence of an abdominal mass due to subperitoneal hemorrhage and the passage of blood by rectum Differentiation is aided by (a) a purpuric rash on the body, usually on the extensor surfaces of the extremities, (b) petechiae produced by a tourniquet test, (c) the platelet count and (d) the age of the patient (abdominal purpura rarely appears in children under the age of 5 years, while most patients with intussusception are under the age of 2 years)

The subperitoneal hemorrhages commonly seen in cases of abdominal purpura may predispose to the development of intussusception, 9 instances having been collected from the literature by Bailey²⁹ If reasonable doubt exists it is certainly wise to consider the condition intussusception and explore the abdomen at once

Treatment—It is now generally agreed that the safest and most satisfactory method of handling intussusception is surgical intervention as soon as possible after the diagnosis has been made, provided the general condition warrants operative intervention Some still recommend, in cases of early involvement, rectal injections as a preliminary to surgical reduction The danger of this procedure lies in subsequent belief that the intussusception has been relieved when in reality the small initial portion of the intussusceptum has remained unreduced The six hours lost before this mistake is appreciated may mean the difference between a simple operative reduction and resection with its high attendant mortality

The surgeon must constantly remember that intussusception is essentially acute intestinal obstruction. We believe that restoration of the fluid balance before operation is most important and prefer to administer lactate-Ringer (Hartman's) solution subcutaneously. This can be done while the operating room is being prepared for use. Gastric lavage is also an important preoperative measure, since removal of the usual retained fluid curbs vomiting with the hazard of pulmonary aspiration.

Ether given by the open drop method is the anesthetic of choice but both the amount used and the total time taken should be reduced as much as possible. The surgeon and his assistant should be scrubbed and ready to operate before administration of the anesthetic is begun, so that no time may be lost. The incision is placed to the right of the umbilicus, and sufficient exposure is obtained to permit introduction of the two index fingers. The tumor is located, and reduction is carried out within the abdomen by milking the intussusceptum backward through the intussusciens until the tight edematous ring marking the origin of the intussusception is reached. It is best at this point to deliver the bowel into the wound, this is usually accomplished without great difficulty. The reduction is then completed under direct vision, and in the absence of any specific etiologic factors the abdomen is closed. Tacking the cecum to the lateral peritoneal wall is not considered necessary or wise, since the incidence of recurrence is low and this procedure is opposed to physiologic principles. If Meckel's diverticulum is an etiologic factor it should be removed, but routine appendectomy is not to be advised. Double intussusception has occasionally been observed and its possibility should not be overlooked.⁶

In cases in which operation is performed early surgical reduction is usually easy. If many hours or several days have elapsed reduction may be extremely difficult or impossible. In such a case one may wrap a warm, moist sponge about the intussusception and apply gentle pressure with the grasping hand. After some of the edema has been driven out of the tumor mass, reduction may be possible. One is never justified in exerting traction on the distal portion of the colon, because of the great danger of tearing the bowel. If all efforts fail to accomplish reduction, one is left with the choice of either a resection or a colostomy.

Factors in Mortality—The mortality in any large series of cases ranges from 15 to 45 per cent and is almost directly proportional to the delay in surgical treatment. The large number of patients who die come to operation late when the condition requires either extensive manipulation of the intestine or resection. Wade,³¹ with an extensive personal experience in the management of this condition, reported a mortality of 14.06 per cent in a series of 519 cases. That the mortality can be greatly reduced by prompt diagnosis and earlier operative inter-

vention is indicated by Hudson's¹⁰ recently reported series of 60 consecutive cases with no mortality. The 1 death in our series of 4 cases occurred twenty-four hours after operation and was due to bilateral diffuse bronchopneumonia.

PNEUMOCOCCIC AND STREPTOCOCCIC PERITONITIS

Incidence and Portal of Entry—Pneumococcic or streptococcic peritonitis is the third cause of acute abdominal disease requiring operation in infancy and childhood. Table 5 shows these two types of peritonitis to be responsible for from 2 to 4 per cent of admissions for acute abdominal disease requiring operation. In our own series the incidence was 3.3 per cent.

In 1922, McCartney and Fraser³⁷ reported 56 cases of pneumococcic peritonitis in children under the age of 12 and from their clinical and operative findings concluded that the infection was genital in origin. Subsequent reports³⁸ have suggested that organisms may enter through the respiratory tract, the intestine or the blood stream as well as through the genital tract. Cole,³⁹ from his experience at the St. Louis Children's Hospital, also concluded that the infection may enter by more than one route. The frequent association of an active or subsiding infection of the upper respiratory tract has been suggested by Swartz⁴⁰ and Newell^{38b} as indicating a likely point of entrance in most patients.

Both sexes are susceptible to pneumococcic or streptococcic peritonitis, although pneumococcic infection is found in a larger percentage of girls than of boys. Streptococcic peritonitis is much more common in the age group from birth to 3 years. Pneumococcic infection is seen more commonly in older children.

Symptoms and Course—The clinical picture in each instance is characterized by abdominal pain, fever, persistent vomiting and frequently diarrhea (table 6). Localization of the pain is not the rule, but the frequent presence of tenderness over the right lower quadrant of the abdomen suggests strongly the possibility of appendicitis. Rigidity is not common and is a variable finding. The temperature ranges from 102 to 104 F., and leukocyte counts from 20,000 to 40,000 per cubic millimeter are commonly noted.

37 McCartney, J. E., and Fraser, J. Pneumococcal Peritonitis, *Brit J Surg* 9:479, 1922.

38 (a) Gordon, H. Acute Suppurative Peritonitis, in Blumer, G., and Ivy, C. G. *The Practitioners Library of Medicine and Surgery*, New York: D Appleton-Century Company, Inc., 1935, vol. 7, p. 407. (b) Newell, L. T., Jr. Primary Streptococcus and Pneumococcus Peritonitis in Children. *Surg Gynec & Obst* 68:760, 1939. Fraser¹².

39 Cole, W. H. Pneumococcic Peritonitis, *Surgery* 6:386, 1937.

40 Swartz, J. Primary Streptococcic Peritonitis in Children, *Surg Gynec & Obst* 45:590, 1927.

TABLE 5.—*Peritonitis in Childhood Due to Pneumococcus and Streptococcus Analysis of Clinical Data*

TABLE 5— <i>Pentontis in Childhood Due to Pneumococcus and Streptococcus</i>														
Author	Year	Organism				Boys	Girls	Average Age	Primary Infection			Treatment		Mortality, Per centage
		Cases	Strepto	Pneumo	coccus				Genital Inact	Throat	Chest	Blood Stream	Con servative	
Lamm ⁷	1921	10	10	0	0									7
McCartney and Irace ⁸	1922	56	0	0	0	12	11	6	36	18	terminal		56	65
Beckman ⁹	1923	18	1	14	3	3	10			2	terminal		18	65+
Inschutz B and Iowenburk H. Pneumococci and Streptococci Peritonitis, J A M A 56: 99 (Jan 9) 1920	1920	22	9	17	3	3	17	1.6	3	22	9	1	18	100
Cohen ¹⁰	1927	9	6	3	3	6	3	2.6		9			9	80
Swartz ¹¹	1927	11	11	0	5	5	9	85% 1.5	2	10	2		11	79
Idd ¹²	1930	51	36	15								1 averted	Delayed operation	61
Hudson ¹³	1931	29							Usual		terminal	1 averted	Delayed operation	
Gordon ^{14a}	1931	10	11	9	17	23	23	1.6	2	23	All terminal		10	51
Nowell ^{14b}	1939	61	21	36	39	22	22	1.6	0	2.2%	Common	1 averted	Delayed operation	78.5

TABLE 6—*Pneumococcic Peritonitis in Infancy and Childhood Analysis of Clinical Data*

TABLE 6 — <i>Pneumococcus</i>																		
Author	Cases	Average Age	Boys	Girls	Severe Emesis	Diarrhea	Fever	Average White Blood Cells	Peritonitis			Origin of Infection			Positive Peritoneal Puncture	Treatment		Mortality, Percentage
									Primary	Secondary	Throat	Chest	Genital	Kidney		Conservative	Immediate Operation	
McCartney and Fraser ³⁷	56	6	14	44	++++	+++	104 F +	33,000	33	18	18	36			Terminal	56	65	
Beckman ⁸	14	Under 6	1	13	++++	+++	104 F +	20,000 to 40,000	13	2	2		5	13	5	13	100	
Ipschutz, B., and Iowenburs, H.	13	1 6	1	12	++++	+++	104 F +	32,000										
Pneumococcic and Streptococcic Peritonitis in Infancy and Childhood, I. A. M. A 86 99 (Jan 9) 1923																		
Cohen ⁶	3	2 4	0	3								5		4		Favored	66	
Ladd ⁵	15				++++	+++	104 F +	High			24	8	0	16	17	Favored	61 1	
Gordon ^{34a}	9				++++	+++	102 F +	20,000 to 40,000	12								0	
Newell ^{34b}	23	1 10	22	14	++++	+++	102 F +						2	0	0	Yes	Delayed	
McLaughlin and Davis (this paper)	2	4			++	+++	102 F +	30,000	2									

The acute fulminating condition progresses rapidly to generalized peritonitis with marked prostration and early death, particularly with the streptococcic infections, mortality figures vary from 90 to 100 per cent. In a certain percentage of cases pneumococcic infection tends to localize, with the development of an abscess after a few days. Such a collection of pus may be found anywhere within the abdomen but is usually located in the pelvis. In both of our cases the involvement was of this type, and complete recovery followed drainage of the abscess.

Treatment—The treatment of patients with primary peritonitis has been a matter of controversy for many years. Surgeons have been divided into two groups, one favoring early operation with drainage of the pelvis and the other recommending conservative measures until a localized abscess develops.

No definite course can as yet be accepted as best. Frequently the decision to carry out early operation is made because the presence of acute disease of the appendix cannot be adequately ruled out. In this problem peritoneal puncture is of the greatest value. If a few drops of pus can be obtained and the offending organisms identified, one feels more justified in pursuing an expectant course.

The use of specific serums for primary peritonitis has been the most encouraging recent advance in the treatment of the pneumococcic condition. Newell^{35b} has recently reported the use of antipneumococcic rabbit serum with prompt recovery in 1 case and has stated the belief that this form of therapy may be of great value. As yet no data are available on the use of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) for this type of pneumococcic infection. Probably, through advances in specific treatment, reduction in mortality will be achieved, since a consistently high mortality follows all forms of surgical treatment with simple supportive measures in cases of acute diffuse involvement.

There are not as yet sufficient available data to enable one to evaluate the therapeutic effect of sulfanilamide in the treatment of streptococcic peritonitis. However, there is good reason to believe that the drug may be a valuable agent in the treatment of this condition which now has an appallingly high mortality.

SUMMARY AND CONCLUSIONS

No attempt has been made to consider all the various lesions which may produce acute conditions of the abdomen requiring operation in infancy and in childhood. The purpose has rather been to stress the four most common causes and to present our own experience in the management of these. An effort has been made to review the important recent literature on the subject and to correlate the experience and conclusions of the various authors.

SUPERNUMERARY BREAST

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The development of the supernumerary breast (polymastia or hypermastia) and its modality constitutes an interesting chapter in clinical observation. The subject is of clinical interest because of the differential diagnosis of supernumerary breasts and lipomas and other benign tumors and because of the discomfort caused by the swelling of aberrant breast tissue during pregnancy and childbirth. It is also important to establish that there is no evidence that carcinoma develops more frequently in these formations than in normal breasts.

There are in the literature almost six hundred references to congenital anomalies of the breast. In the human being the supernumerary organs develop either in the milk line or in locations that are atypical for human beings but normal for other mammals. A short sketch of the embryology and comparative anatomy may therefore be of interest, in addition to a description of some new cases and a summary of cases collected from the literature since the extensive study by Deaver and McFarland in 1918.

EMBRYOLOGY

According to the observations of Basch, Neumann, Schultz, Schmidt, Kallius and others, two lines of thickened epithelium running parallel to each other and longitudinally on the ventral surface appear first in the 4 mm embryo. This anlage develops uniformly from the axilla to the pubic region and ends at the inside of the thigh (fig 1). In the 10 mm embryo the milk lines measure about 2 mm in length and can be seen with the naked eye. With further development there is definite localization of epithelial cells in molehill formation at the level of the fourth rib, from which later the normal breast develops. The epithelial cells conglomerate at this level, gradually increase in volume and penetrate to the subcutaneous tissue. The first epithelial buds which will form the gland proper, as well as the epithelial prolongations which increase in size and form the primitive breast, appear in the 170 mm embryo. In the 45 cm fetus well developed ducts are present, opening to the future nipple, which is still under the level of the skin and remain there until after birth. In the normal person the milk line gradually

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disappears with the exception of the anlagen for the normal breasts. The occasional failure of this process of extinction accounts for the formation of breasts at other locations on the milk lines.

Some authorities, particularly Champneys, have stated the belief that supernumerary mammary glands are enlarged sweat glands and not true breasts. Champneys' theory was supported by Tandler's observation of a patient in whom there was complete failure of development of the breast and nipple, together with total absence of sweat glands all over the body and partial absence of the sebaceous glands.

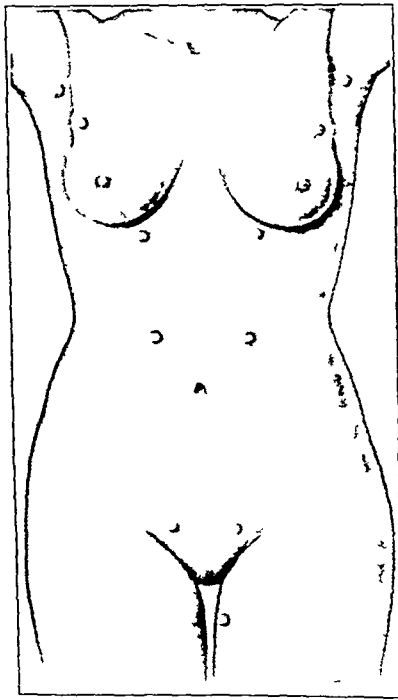


Fig 1—Schematic representation of the development of supernumerary breasts in the milk line

COMPARATIVE ANATOMY

It was Geoffroy-Saint-Hilaire who, in 1836 suggested that man was descended from animals having multiple breasts. Darwin later subscribed to this theory. In his "Descent of Man" in 1871 he called attention to the fact that supernumerary breasts should be considered an atavistic manifestation.

Phylogenetically, inguinal breasts are found in the pouched mammals (monotremes and marsupials) as well as in the ungulates and cetaceans. In elephants, sirenia, bats of some types and most of the primates, breasts are confined to the pectoral region as is also the case in some

rodents, e g the jumping hare (*Pedetes cafer*) Axillary breasts develop normally in the fruit bats and the flying lemur Mammæ are found in the inguinal region in one of the lemurs of Madagascar, in the axillary region in the gentle lemur (*Haplemur*) and behind the axilla in the hutia (*Capromys pilorides*) The porcupine has a mammary gland on the anterior side of each axilla, in the nutria (*Myocastor*) the mammæ are placed behind the scapula, while in the cetacea (whale, porpoise, dolphin) they are placed on the labia of the vulva The viscaccia (*Lagostomus maximus*) and some other rodents have breasts on the dorsolateral aspect of each thigh In the opossum there is commonly a breast in the midline of the abdomen and thorax, in addition to numerous other mammæ

According to Hartman, the largest number of breasts found in animals is in the South American marsupial (*Monodelphus henseli*), which has twenty-five, and in the insectivore tenrec of Madagascar (*Centetes ecaudatus*), which has twenty-two pairs The latter is probably the most prolific of insectivores, as many as twenty young being brought forth at one birth Among the primates, not only human beings but anthropoid apes (though perhaps less frequently) have supernumerary breasts Aside from reports of a few unilateral nipples (reported by Hartman), Coolidge first recorded a case of symmetric supernumerary mammæ in a chimpanzee

Total absence of breasts (amastia) is a true agenesis, that is, total absence of the development of the milk anlage, which is a rare condition It is usually accompanied by other malformations of the soft parts or bones In addition to the cases collected by Deaver and McFarland, amastia has been observed by Fabre, Glos, Louria, Putzu Doneddu, Stiglbauer, Szczawinska and Velasco Blanco and Echegaray

In this paper the discussion will be limited to the incidence, physiology and pathology of the supernumerary breast

INCIDENCE

There are apparently some racial differences in the incidence of polymastia The abnormality is of more frequent occurrence among Japanese women (5.19 to 6 per cent) than in the men (1.68 to 2.03 per cent), according to Iwai For Chinese men the figure was given as 3.6 per cent by Takeya It is also observed more frequently above the normal breast in the Japanese than in the white race, occurring above in approximately 70 per cent of the cases and below in 30 per cent The figures are approximately reversed for white people

Supernumerary breasts are unilateral or bilateral If multiple, they usually occur in the milk line Atypical locations have been described in great detail by Deaver and McFarland, who collected instances from the literature up to 1915, and by other observers

One additional breast occurs in from 60 to 65 per cent of the cases, two in 30 to 35 per cent, three in 3.5 to 4 per cent and four in 1.5 to 2 per cent. It is clear, therefore, that the relative incidence of super-

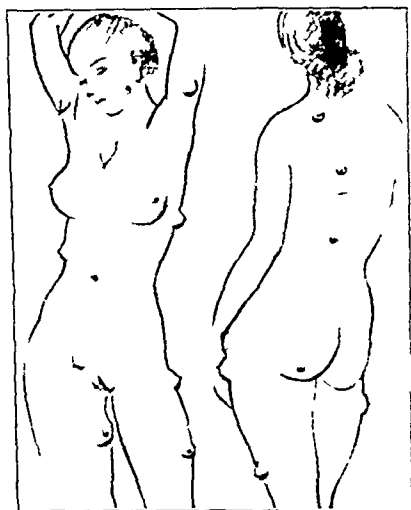


Fig 2—The location of "atypical" supernumerary breasts, schematically shown, as observed in females by different authors

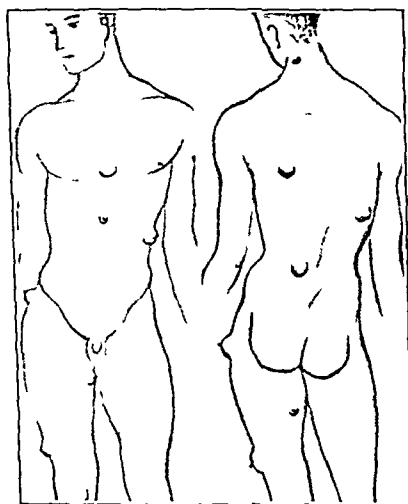


Fig 3—Location of "atypical" supernumerary breasts, schematically shown, as observed in men

numerary breasts diminishes with the increase in the number of those organs observed in one person. There is reported a case of eight breasts in a male (Wiedersheim) and another of eight in a female (Dietrich)

Hirst observed nine in a colored woman, four of them being large enough to afford nursing and all secreting milk after childbirth. In Graham-Campbell's case there were ten breasts and nipples in a woman, and the four cephalic ones were equal in size and shape. The newborn child of this woman also had a supernumerary nipple, which supports the opinion of most observers that the condition is hereditary. Neugebauer observed a woman with ten breasts situated in the milk lines

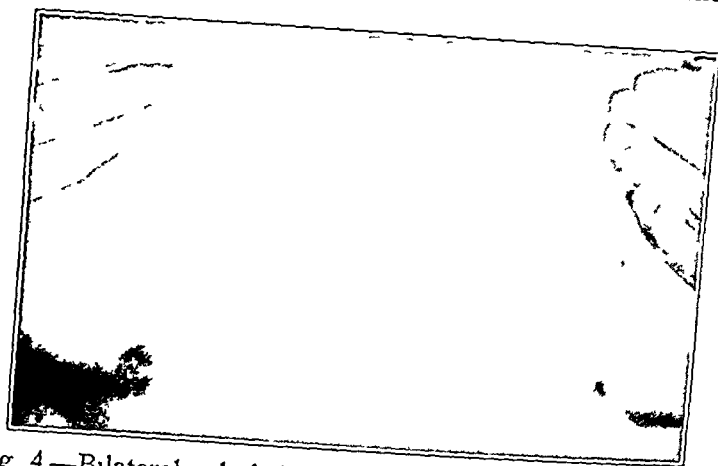


Fig 4—Bilateral polythelia in the milk line beneath the breast



Fig 5—Intra-areolar polythelia in a white woman

which were all functional after parturition. In this case three pairs were situated above the normal breasts.

Aberrant breast tissue is observed relatively frequently and almost exclusively in the axillae. These masses are usually noted at pregnancy. But Schmidt-Tannwald observed such tissue, the size of a man's palm, beneath the clavicle of a woman. In my series there were 41 patients with aberrant breast tissue, all women and all with the tissue in the axillae. In 11 of the patients who were treated by surgical procedures the character of the tissue was proved by pathologic examination.

Polythelia is found with relative frequency. The figures vary widely according to different authorities. It occurs in equal numbers of persons in the two sexes, the incidence varying up to 6 per cent, although a range of from 14 to 23.3 per cent has been suggested by published figures. A conservative estimate of from 1 to 2 per cent seems to be more exact.

Unusual is the form of intra-areolar polythelia which may originate, according to Sutton, as the result of intrauterine division (dichotomy) of the developing breast or nipple. Though of rarer occurrence, polythelia may be confined to a single breast, two, three or more nipples.

*A Compilation of Atypical Cases of Supernumerary Breasts Observed
by Various Authors*

Location of Supernumerary Breasts	Number of Patients	Sex of Patient	Authors of Case Reports
Cheek	2	Female	Deaver and McFarland
Neck	1	Male	Holtz
Ear, tragus and helix	2	Female	Hug Barth
Arm, upper part of left	1	Female	Sato
Thorax and abdomen (midline)	9	4 male 5 female	Compiled by Deaver and McFarland
Shoulder	3	2 male 1 female	Hoepfner Scalzi Klob
Back lumbar region	9	5 male 4 female	Compiled by Deaver and McFarland Jaki
Pubic inguinal region	10	4 male 6 female	Compiled by Deaver and McFarland
Flank and hip	4	3 male 1 female	Compiled by Deaver and McFarland
Thigh and Scarpa's triangle	9	5 male 4 female	Testut Steinborn and Mosig Dietzky Romiti Sacasa Cu tore Forster de Cholnoky
Thigh and dorsolateral aspect	7	3 male 4 female	Compiled by Deaver and McFarland
Buttock	1	Female	Compiled by Deaver and McFarland
Vulva	4	Female	Bergner Purves Mengert
Labium majus	1		
Labium minus	1		

having been thus noted, and report has been made of these supernumerary nipples on both breasts in the same person. One of my patients had such an intra-ocular polythelia, as shown in figure 5.

ATYPICAL LOCATIONS OF SUPERNUMERARY BREASTS

Supernumerary breasts develop regularly in the embryonic milk lines, but they may also be found, more rarely, at locations which are normal in certain other mammals. These atypical, "freak," aberrant breasts fundamentally arise on a foundation of misplaced embryonic anlage. Accepting the Geoffroy-Saint-Hilaire-Darwin theory, the observation of such abnormalities would prove the reversion to ancestral characteristics that is called atavism.

I have made a study of atypical cases observed by different authors and present the accompanying table.

HEREDITY

Klinkenfuss recorded a hereditary incidence through four generations, and Bukenfeld, among others, observed the condition in twins. By selective breeding in sheep, Bell succeeded in breeding out four functional supernumerary breasts in the offspring. He considered this proof of their hereditary character.

Though Astarte, the goddess of fertility, was represented as many breasted, and in spite of the popular belief that women with polymastia have multiple births, there is not sufficient evidence to support this expectancy. Apparently polymastic women do not show a tendency to bear twins more frequently than do other women.

CLINICAL ASPECTS

Kajava classified congenital supernumerary breasts as

- (1) complete breast with nipple, areola and gland tissue,
- (2) supernumerary breast without areola but with nipple and gland tissue,
- (3) supernumerary breast without nipple but with areola and gland tissue,
- (4) aberrant gland tissue without nipple and areola,
- (5) pseudomamma with nipple and areola but without gland tissue (the breast tissue is replaced by fat),
- (6) polythelia (the presence of nipples only),
- (7) polythelia areolaris (the areola only),
- (8) polythelia pilosa (only a patch of hair present)

Supernumerary breasts usually appear as polythelia or pseudomamma. Complete supernumerary breasts are exceptional. Perfect supernumerary breasts may secrete milk during the period of lactation and undergo the cyclic changes of the normal breast. Tumors may develop in them.

An interesting case was reported by Bergner. A 27 year old woman at repeated pregnancies acquired a cyst on the right labium, which at one time yielded 250 cc. of what proved, on analysis, to be milk. Such findings were also described by Purves and Mengert in a patient in whom the labium minus was involved. McFarland pointed out that the appearance of a supernumerary breast in this location is another form of atavism, as in the cetaceae all mammary rudiments disappear with the exception of one in each labium majus.

My observation of a well developed complete breast in Scarpa's triangle (on the right thigh) seems to be unique among available recorded cases and comparable only to a case of pseudomamma in the same location in a man reported by Forster (fig. 6). A similar case

was observed in which a man had a pseudomamma on the inside of the right thigh where the milk line ends

Our case may be summarized as follows

E. C., a woman aged 42 complained of a lump on her right thigh which she said she had had as long as she could remember. It increased in size during pregnancies, was not painful and did not secrete. Menstruation had begun at the age of 13 and was of the regular twenty-eight day type. She had had two children and two miscarriages. Examination revealed a well developed breast (like that of a girl of 16) with a large well developed nipple located on the inner aspect of the upper part of the right thigh (figs 7 and 8). On palpation it had the character of somewhat firm but normal breast tissue. The patient returned for examination two months later, complaining of occasional lancinating and pricking pain in this breast, which was more marked before menstruation. Mastectomy was advised but refused.

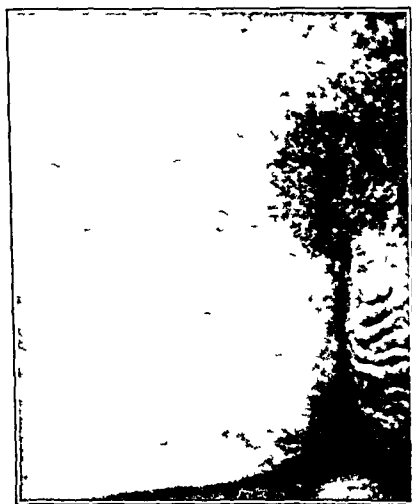


Fig 6—Pseudomamma in a man (Forster)

It is of clinical interest that these malformations may annoy the bearer by their physiologic function and may give rise to benign and malignant tumor formation. Those located in the axilla most frequently give rise to complaints (fig 9). The woman may become aware of this misplaced breast during pregnancy and lactation, when swelling and milky discharge (if ducts are present) occur. The swelling is accompanied by pain, sometimes severe, usually in both axillas. In some cases the aberrant gland tissue is connected by a duct with the normal breast, and the secretion may be discharged through the main channels. In such a case subjective complaints will be less. If no such communication exists, the swelling and pain will be more marked. These round or often spindle-shaped or oval swellings are very tender, appearing usually between the second and the fourth day after delivery and increasing in



Fig 7—Lateral view of a complete supernumerary breast at Scaipa's triangle on the right thigh of a white woman

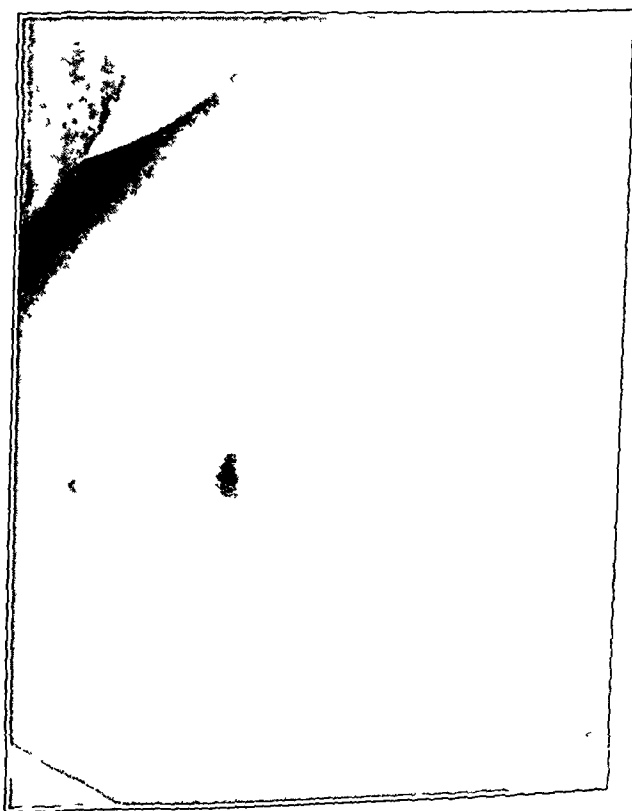


Fig 8—Direct view of supernumerary breast shown in figure 7. Note the well developed nipple and areola

size up to the fifth or seventh day. If a duct is present, there may be secretion of colostrum or milklike fluid. (According to Seitz these functional tumors are not true supernumerary breasts but large sweat glands of the axilla undergoing the described changes under the stimulus of pregnancy.) There is no ground for surgical intervention in such cases unless infection has taken place or unless persistent secretion keeps the patient's clothing wet and the patient desires to have the 'tumor' removed.

DIFFERENTIAL DIAGNOSIS

This condition must not be confused with the relatively frequent prolongation of a tail of the normal breast which gives the impression, on superficial examination, of being aberrant breast tissue.

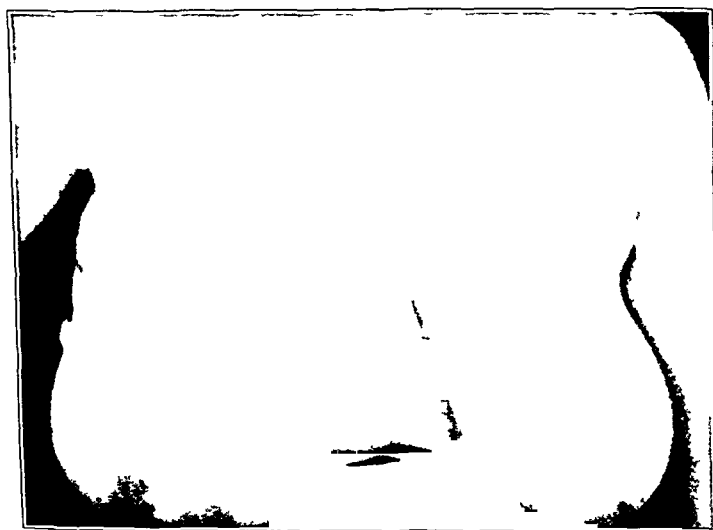


Fig. 9—Bilateral aberrant breast tissue in the axilla

Aberrant breast tissue is frequently diagnosed as lipoma since it is sometimes totally composed of fat tissue. More often it appears as a soft, lobulated fatty tumor enclosing a small core of breast tissue, which may be only a few millimeters in diameter. In the cases of 4 of my 11 patients who were operated on the condition was diagnosed clinically as lipomas, and in these cases the pathologic report was aberrant breast tissue. The patients were women about 25 years of age who did not present characteristic symptoms, such as cyclic changes. The report of 1 of these cases follows:

F. H. a woman 31 years of age had noticed a small lump in the left axilla at the time of childbirth, four years before the examination. During the last year persistent swelling and lancinating pain had been present. Examination revealed a soft, lobulated well circumscribed tumor about 8 cm. in diameter. A clinical

diagnosis of lipoma was made, and the tumor was excised. Pathologic examination showed low grade inflammation with cystic changes of the aberrant breast. Post-operative recovery was normal, and the results of follow-up examination were negative.

From the diagnostic point of view, supernumerary breast tissue may be confused with other benign tumors, as in 2 of my cases. In 1 of these the growth proved to be a fibroma (fig 10) below the normal breast in the milk line, in the other, a lipoma in the axilla. The latter growth impressed me as being a functional chronic mastitis, accompanied by occasional menstrual pain, in a woman 36 years of age. In my opinion the clinical diagnosis should always be fortified by a pathologic report.

The diagnosis of supernumerary breast tissue is confirmed if the patient states that the swelling appeared simultaneously with develop-

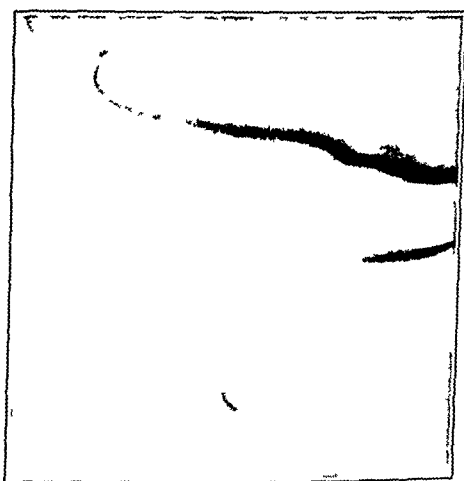


Fig 10—A fibroma which resembles a supernumerary breast

ment of the normal breast at puberty or that it appeared at the time of pregnancy or childbirth. It may follow the cyclic changes of the normal breast, that is, there may be premenstrual swelling with some tenderness.

TUMOR FORMATION IN THE SUPERNUMERARY BREAST

Tumor formation is observed in the supernumerary breast when glandular tissue is present. It is relatively most frequent in the aberrant breast tissue. Occasionally cystic degeneration in such breasts has been observed (Noronha).

Fibroadenoma was observed in 1 of my cases.

T. S., a 25 year old woman, complained of a lump in the right axilla which had appeared one and a half years before. Occasional pain was present, and the tumor slowly increased in size. Six months after its discovery the growth was removed, and a year later in the follow-up examination recurrence was noted.

Examination showed a smooth, oblong, movable subcutaneous mass, 3 by 3.5 cm in diameter, slightly elevated, firm, slightly lobulated and not tender on palpation. By elliptic excision the old scar with the multilobular white tissue growth was removed. The mass gave the impression of being supernumerary breast tissue. The pathologic examination showed intracanalicular fibroadenoma of the supernumerary breast. This case illustrates the importance of thorough dissection on the first operation, in order to prevent recurrence.

White excised a fibroadenoma from one of two bilateral supernumerary breasts located beneath the normal breasts. Palumbo found one fibroadenoma in the axilla, with a coincident myxosarcoma of the breast. Friedel reported a case of fibroadenoma in the vulva, and Roth observed cystic fibroadenoma in the same location, both developing in supernumerary breast.

Carcinomatous degeneration was observed in the aberrant axillary breast by Giacobbe and Matti and in aberrant breast tissue beneath the clavicle by Ravdin. Erdmann observed it in his 3 cases, in 1 of which the patient was a man of 26. Patel, Montemartini and Greene have reported carcinoma of the vulva developing in supernumerary breast in that location. In 1929 Razemon and Bizard collected 43 cases, 28 of the growths were in the axilla, 10 in the sternal region and 5 under the clavicle, in addition, there were 23 benign tumors in the supposedly supernumerary breasts, of which 19 were in the axilla.

On the other hand, Biancheri found only 31 cases in the literature as of 1932, some of which might be duplications of those reported by Razemon and Bizard. I am under the impression that many such cases should be classified as instances of "carcinoma of the breast" unless direct connection between the normal breast and the aberrant tissue can be eliminated with certainty.

The relatively rare observations of benign or malignant tumor formations in these frequently occurring anomalies give the impression that the anomalies are essentially harmless.

TREATMENT

The study and observation of the supernumerary breast are interesting because they give a clue to the line of human descent and form an interesting chapter of comparative anatomy, but a survey of all the cases presented in the literature leads to the conviction that it is a harmless malformation. Therefore, unless the breast has an inconvenient function (such as a discharge) or an inconvenient location (for example, at the axilla), or unless the patient has subjective symptoms (such as a feeling that she is like an animal) or there is a tumor formation present, no surgical intervention is indicated.

SUMMARY

The development of the supernumerary breast may be considered a reversion to remote ancestral characteristics (atavism)

Accessory breasts are commonly observed (1 to 2 per cent) in both sexes and are usually situated in the milk lines. They are also rarely found at atypical locations where lower mammals have normal breasts. A compilation of atypical supernumerary breasts in human beings is reported.

Two new cases of unusual supernumerary breasts are described, 1 of a complete breast in a female and the other of a pseudomamma in a male, in both cases the growth was situated on the inner aspect of the right thigh. One case of infrequently observed intra-areolar polythelia in a multipara is also described. Two tumors of the accessory breasts surgically treated proved, on pathologic examination, to be chronic mastitis and fibroadenoma, respectively. No malignancy was found in any of the 41 cases of functional supernumerary breasts.

No operation is indicated for these anomalies unless there are "psychologic" symptoms or unless their location or tumor formation warrants removal.

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EPIDURAL HEMANGIOMA ASSOCIATED WITH HEMANGIOMA OF THE VERTEBRAE

REPORT OF A CASE

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CARL W RAND, MD

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LOS ANGELES

In the experience of Aschoff,¹ Kaufman² and others, hemangiomas of the vertebral column have been encountered rarely. In 1927, however, Makrycostas³ was able to describe 12 cases which he collected during the routine autopsy work of Erdheim's laboratory. He stated the opinion that the uncommon occurrence of compression of the spinal cord with such lesions probably explains the infrequency of reports of the condition in the literature. No neurologic manifestations were recorded in the 12 cases which he described. He observed that vertebral hemangiomas are most common in late adult life, are irregular in their distribution, are most frequently multiple and are ordinarily discovered in the lower dorsal and lumbar vertebrae.

In 1928 Topfer⁴ more than confirmed the impression of Makrycostas that hemangiomas of the vertebral column are not so much a pathologic as a clinical rarity. He sagittally sectioned the vertebral columns of 2,154 cadavers at necropsy, and in 257, or 11.93 per cent, found angiomas of the vertebrae, although in 4 cases tumors were in the spinous processes and in 3 others in the arch. Incidentally, in 9 of the necropsies angiomas were discovered in the sternum, in 3, in the femur, in 3 others, in the skull, and in 4 others, in the liver. None of the tumors

From the Children's Hospital

1 Aschoff, L. *Pathologische Anatomie*, ed 6, Jena, Gustav Fischer, 1923, vol 2, p 226

2 Kaufman, E. *Lehrbuch der speziellen pathologischen Anatomie für Studierende und Aerzte*, Leipzig, Walter de Gruyter & Co, 1922, vol 1, p 937

3 Makrycostas, K. Ueber das Wirbelangioma, -lipom und -osteom, *Virchow's Arch f path Anat* **265** 259, 1927

4 Topfer, D. Ueber ein infiltrierend wachsendes Hämangiom der Haut und multiple Kapillarektasien der Haut und inneren Organe. *Zur Kenntnis der Wirbelangiome*, Frankfurt Ztschr f Path **36** 337, 1928

produced any known symptoms, which is readily understood when it is realized that in no case did they extend into the spinal canal. As might have been expected, variation in size of the growth from complete involvement of the vertebral body to a small tumor the size of a pea occurred. In 41 cases the angiomas were associated with lipomatous formation.

In 1929 Bailey and Bucy⁵ pointed out that although cavernous hemangiomas of the vertebrae present a characteristic roentgen picture which can be diagnosed in none of the 11 cases reported in which there were symptoms referable to the spinal cord was the diagnosis made either before operation or before necropsy.

That epidural hemangiomas seldom occur is evident from the fact that Johnston⁶ in 1938 was able to collect only 14 cases. He apparently overlooked 1 reported by Bucy⁷ and 2 of Dott's mentioned by Bucy,⁸ which bring the total to 17. Though there may be others which have been neglected, the number remains small. Instances of hemangiomas of the vertebrae associated with hemangiomas of the spinal cord and its membranes have been reported only exceptionally. In 1 such case an unsuccessful operation was done by Elsberg (Globus and Doshay⁸). In many ways the following case, which was observed at the Children's Hospital of Los Angeles and in which the correct diagnosis was made preoperatively, seemed similar. To our knowledge the growth described here is the third vertebral hemangioma to be treated successfully by operation. It is, moreover, the only hemangioma of the vertebrae with compression of the spinal cord diagnosed preoperatively as such.

REPORT OF CASE

Schoolboy 14 years of age. Numbness of the feet and unsteadiness of gait Dec 15, 1938, becoming progressively worse. Sensory level at eighth thoracic area with complete spinal subarachnoid block and highly elevated values for protein. Pain to palpation over seventh and eighth thoracic spines. Several scattered pigmented hemangiomatous nevi especially in the region of fifth to ninth thoracic dermatome. Preoperative diagnosis of epidural vertebral hemangioma confirmed by laminectomy and histopathologic study. High voltage roentgen therapy. Recovery.

⁵ Bailey, P. and Bucy, P. C. Cavernous Hemangioma of the Vertebrae, *I. A. M. A.* **92** 1748 (May 25) 1929.

⁶ Johnston, L. M. Epidural Hemangioma with Compression of the Spinal Cord. *I. A. M. A.* **110** 119 (Jan 8) 1938.

⁷ Bucy, P. C. Blood Vessel Tumors of the Spinal Canal, *S. Clin. North America* **12** 1323 (Oct.) 1932.

⁸ Globus, J. H., and Doshay, L. J. Venous Dilatations and Other Intra-spinal Vessel Alterations Including True Angiomata with Signs and Symptoms of Cord Compression. *Surg. Gynec. & Obst.* **48** 345 (March) 1929.

Clifford F., a schoolboy aged 14, was admitted to the Children's Hospital on Jan 21, 1939. He had been well until noon of Dec 15, 1938. At this time he became unsteady on his feet, his right leg being noticeably more ataxic than his left. A few nights later he realized that he was unable to feel the bedclothes normally over his lower extremities, and he also noticed that his feet felt rather numb. This numbness became progressively more pronounced, so that within a week of his admission to the hospital it had extended up to his waist. A few weeks after the onset of his illness he realized that his legs felt stiff and that he had difficulty in relaxing them. This spasticity increased, as did the ataxia, so that a few days prior to hospitalization he was able to walk only with difficulty. A few weeks after the onset of his illness he noticed occasionally a shocklike sciatic pain down both thighs when he sat up suddenly. Occasionally this was limited

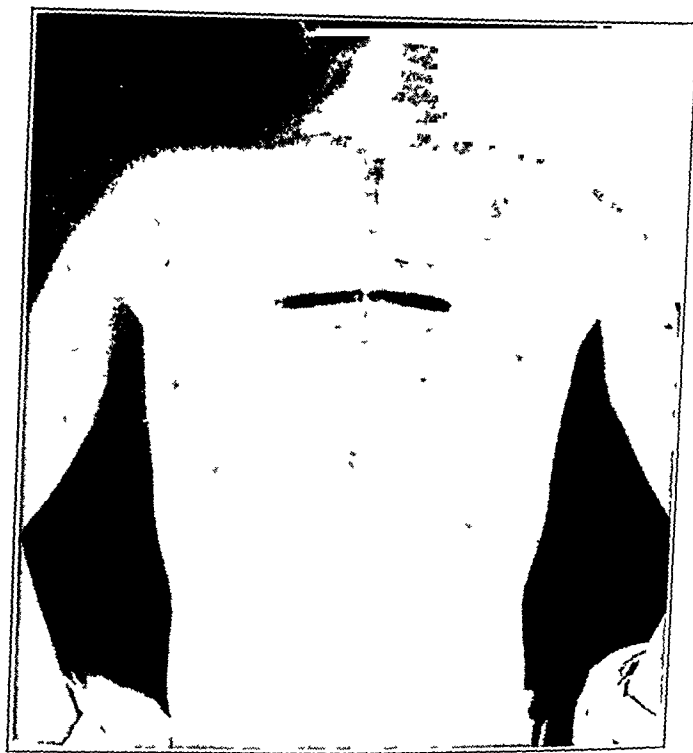


Fig 1—Photograph taken postoperatively of the patient's back, showing the scattered pigmented nevi. The pencil marking on the skin is over the involved area of the vertebrae for the roentgen therapy.

to one side. He failed to notice any accentuation of his symptoms on coughing or straining, and they were unrelated to any injury to his back. His family and past history were entirely noncontributory.

Examination revealed him to be well developed and well nourished. He was mentally alert and cooperative. General physical examination was without positive result except that on the back, especially in the region of the fifth to the ninth thoracic dermatome, several scattered pigmented hemangiomatous nevi were found (fig 1). Tenderness to palpation was also noted over the seventh and eighth thoracic spinous processes. Neurologic examination revealed no significant abnormality of the cranial nerves. Although tests for coordination were performed normally with the upper extremities, there was considerable ataxia when they were carried out with the lower extremities. The Romberg reaction was positive.

and the gait was ataxic, the patient walking spastically on a wide base. A definite level of hypesthesia to light touch, pinprick, heat, cold and vibration, corresponding to about the eighth or the ninth thoracic segment with suggestive sparing of the sacral segments, was obtained. Sensory impairment seemed a little more marked on the right than on the left. The sense of position was completely impaired in the lower extremities. The abdominal and epigastric reflexes were not obtained, the Babinski sign and allied signs were strongly positive bilaterally. The biceps, triceps and radial reflex and finger jerk were bilaterally hyporeactive. An abortive patellar reflex and a sustained ankle clonus were obtained on each side, and both legs were spastic. Compression of the jugular vein caused no sciatic pain or accentuation of the symptoms. No disturbance of the sphincters was evident at this time, and the vasomotor reaction was only moderately accentuated.

Roentgenograms of the thoracic vertebrae taken on Jan 17, 1939, showed decalcification of the body of the seventh dorsal vertebra, with loss of the pedicle, and a shadow in the anteroposterior projection which was felt to be due to a

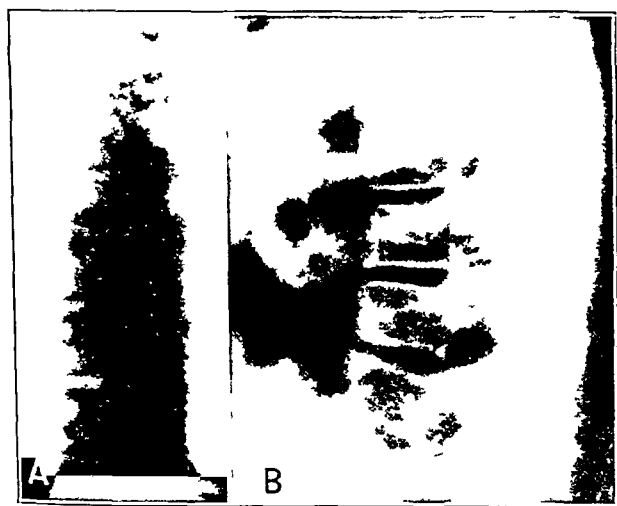


Fig 2—*A*, anterior view of the thoracic vertebrae, showing the vertical striations and loss of the normal homogeneous structure of the seventh thoracic vertebral body. *B*, lateral view of the same structures.

tumor. Other roentgenograms, taken on January 19 (fig 2), were sufficiently clear to lead to the diagnosis of hemangioma of the seventh vertebra. The parallel vertical striations of the vertebral body with loss of the normal homogeneous structure, so characteristic of the picture, though not as prominent as is often seen, were sufficiently evident to be diagnostic.

Examination of the blood on January 13 revealed a hemoglobin content of 81 per cent, a red cell count of 4,200,000 per cubic millimeter and a white cell count of 6,550 per cubic millimeter, with normal-appearing platelets. Urinalysis on January 14 gave negative results for albumin, sugar and Bence Jones protein. Microscopic examination disclosed no red blood cells or casts. A lumbar puncture by Dr T C Welch on January 16 revealed complete block, the spinal fluid gave a negative Wassermann reaction, contained 4 cells per cubic millimeter and had a total protein content of 260 mg per hundred cubic centimeters.

In view of the appearance of the roentgenograms, the level of hypesthesia, the scattered papillary hemangiomatous nevi and the other positive findings, a pre-operative diagnosis of vertebral hemangioma involving the region of the seventh thoracic vertebra with compression of the spinal cord from an epidural hemangioma was made.

A midthoracic laminectomy was performed on January 23, and, as had been anticipated, the skin and underlying tissues were very vascular. The bone of the removed sixth, seventh and eighth spinous processes and laminae was soft and infiltrated with tumor. Hemorrhage was so profuse that anything but partial removal of the vascular extradural hemangioma was precluded. No attempt was made to open the dura, and in view of the findings there seemed no reason to do so. Bleeding was controlled eventually by means of the electrocautery and pieces of muscle. As profuse hemorrhage had been anticipated, a transfusion of 600 cc of citrated blood was given shortly after the operation was undertaken. Closure was carried out in the usual manner, with extradural drainage by means of a Penrose drain brought out through a separate stab wound to one side of the incision. The patient's recovery from the procedure was uneventful, and the wound healed without incident. On the seventh postoperative day, although the sensory level was still present, the boy believed that sensation had improved considerably. He was able to move his legs better and was not so troubled with spasticity. His sense of position, however, was still much impaired. High voltage roentgen therapy was started on the thirteenth postoperative day, and fifteen treatments, totaling 3,000 roentgen units, were subsequently given. On the nineteenth postoperative day the sensory level previously demonstrable had disappeared, and the spasticity had markedly improved. He was still ataxic, however, with bilateral ankle clonus and a bilaterally positive Babinski sign. The sense of position of the lower extremities was still impaired, and the Romberg sign was strongly positive. By the twenty-eight postoperative day, although he was able to walk, he continued to be ataxic, a condition which had improved only slightly at the time of his discharge, on March 3 (the thirty-ninth postoperative day). When he was seen again, on April 9, about seventy-seven days after the operation, he was quite well. He was going to school again, riding his bicycle, and was able to run and walk without any indication of ataxia.

Pathologic Report—The gross and microscopic specimens were examined by Dr. Lucile R. Anderson, of the Children's Hospital. The specimen consisted of a combined piece of bone and cartilage measuring 3.9 cm. in length and up to 1.2 cm. in width, with a piece of dark red, hemorrhagic-appearing soft tissue measuring 1.8 by 2 by 1 cm. and containing spicules of cancellous bone and a portion of attached fatty tissue. The sectioned material revealed plexuses of endothelium lined channels filled with blood lying in a stroma of loose connective and fatty tissue (fig. 3A). Occasional plasma cells and round cells and also a few bone spicules were found in the connective tissue. The picture was felt to be typical of capillary or cavernous hemangioma. A longitudinal section of the specimen of bone showed replacement of the cancellous bone marrow with hemangiomatous tissue similar to that observed in the soft parts (fig. 3B).

COMMENT

From his experience with vertebral hemangiomas Bucy⁹ recovered no information concerning the etiology of these lesions and felt unable

⁹ Bucy, P. C. The Pathology of Hemangioma of Bone, *Am J Path* 5:1 (July) 1929.



Fig 3—A, photomicrograph of the epidural hemangioma, revealing plexuses of endothelium-lined channels filled with blood corpuscles lying in a stroma of loose connective and fatty tissue B similar photomicrograph, taken through a specimen of the removed bone

to decide whether they are neoplasms or vascular malformations. Although they differ undoubtedly from the hemangioblastomas in being relatively benign, slow in growth and not metastatic, they are generally distinguished from mere dilatation of capillaries or venules by their independent growth without regard to the laws governing the distribution of such vessels, and for this reason varicosities, aneurysms and redundant granulation tissue are usually excluded. Ordinarily, hemangiomas are divided into the simple and the cavernous form. The simple, or telangiectatic, form occurs most commonly in the skin as nevi in which the abundant though widened capillaries maintain fairly well their form as tubes with parallel walls. In the cavernous type the character of erectile tissue is approached, with widely dilated, irregular blood spaces opening abundantly into one another but separated by a variable amount of connective tissue. Often it is not clearly apparent where the line of division can be drawn between these two types. According to Bucy⁹ there is no microscopic evidence of malignancy. Mitotic figures are never seen, and the stroma is acellular, loose and fibrous. He expressed the belief that the vertebral hemangioma is a benign, slowly growing tumor mass which, as a result of its presence and growth, produces a characteristic reaction in the bone in which it arises or which it invades. Such changes in the bone, he concluded, are only secondary reactive phenomena.

Most of the accumulating evidence suggests a congenital origin for these tumors. Although the cavernous form usually becomes apparent during the second or third decade, this does not preclude the possibility of its embryonal origin, in fact, in many cases the cavernous form has originated from preexisting birth marks. In a study of 645 patients, Fitzwilliams¹⁰ discovered that 83.2 per cent of the hemangiomas had been observed at birth and that an additional 12.8 per cent had appeared within the first three years of life. In 16 per cent of 108 cases of hemangioma reviewed by Patton¹¹ a history of a similar condition occurring in the family was obtained.

According to Cobb,¹² the subject of the metameric distribution of nevi was first taken up in 1863 by Baerensprung,¹³ who described their topographic distribution and drew attention to their development in definite connection with territories of cutaneous innervation. Because the cutaneous alteration consisted of hypertrophy of the elements in

10 Fitzwilliams, D. C. L. The Etiology of Naevi: Nerve Influence in Their Causation, *Brit. M. J.* 2: 489, 1911.

11 Patton, M. M. Pathology and Treatment of Hemangioma Cavernosum, *Northwest Med.* 5: 121 (May) 1913.

12 Cobb, S. Hemangioma of the Spinal Cord, *Ann. Surg.* 62: 641 (Dec.) 1915.

13 von Baerensprung, F. W. Naevus unius lateris, *Ann. d. Char. Klin.* 11: 91, 1863.

which the peripheral nerves terminated, that is, the pigmented layer of the skin containing the free nerve endings and the blood vessels of the papillary layer also receiving nerve filaments, he stated the belief that the lesion is a congenital one of the spinal ganglions. Etienne,¹⁴ who reviewed the subject in 1897, came to a more or less similar conclusion and felt that a nevus represents an intrauterine nerve lesion. It was not, however, until the publication of Cushing's¹⁵ article in 1906 that it was first suggested that organs other than the skin but in the same segment of nerve distribution could be similarly affected. Cushing¹⁵ included 3 of his own with 3 from the literature in which facial hemangiomas were associated with vascular tumors of the cerebral meninges, and since that time facial hemangiomas and associated intracranial vascular anomalies have been observed and reported frequently.

Although this has been true for facial hemangiomas with associated intracranial vascular anomalies, little can be found concerning such hemangiomas of the trunk associated with intraspinal vascular anomalies. Cobb¹² apparently was the first to report a condition of this sort. In his case hemangiomas of the skin occurred in the same dorsal segment in which an epidural hemangioma was uncovered at operation. The presence of the cutaneous hemangiomas associated with symptoms and signs of compression of the cord at the same level led to a correct preoperative diagnosis of intraspinal hemangioma. As a result of his experience with this case, Cobb¹² concluded that cutaneous nevi are at times diagnostically valuable, when the central nervous system is involved segmentally. He also expressed the opinion that congenital vascular tumors arise from a developmental fault of the central nervous system, which explains their possible occurrence in any of the organs innervated by filaments from that neuromere.

Rand¹⁶ was the second to report a case in which a nevus of the skin of the back led to a preoperative diagnosis of hemangioma of the cord which was confirmed subsequently at operation. As far as can be determined, Johnston⁶ was the third to report a condition of this kind, and we (this paper) are the fourth.

Since the publication of the report by Globus and Doshay,⁸ 7 additional cases of epidural hemangiomas have been reported, bringing the total to 17. In 10 of these laminectomy and removal of the tumor resulted in partial or complete recovery and in 1 case in death. In 6 instances laminectomy was not attempted. Our case raises the total

14 Etienne G. Des naevi dans leur rapports avec les territoires nerveux, *Nouvel iconog de la Salpetriere* 10 263 1897

15 Cushing H. Cases of Spontaneous Intracranial Hemorrhage Associated with Trigeminal Nevi. *J A M A* 47 178 (July 21) 1906

16 Rand, C W. Hemangioma of the Spinal Cord, *Arch Neurol & Psychiat.* 18 755 (Nov.) 1927

number of epidural hemangiomas of the spinal cord to 18 and the total number of those treated by laminectomy with recovery to 11

As far as can be determined, Hitzrot¹⁷ in 1917 first published and described a roentgenogram of a bone hemangioma. In 1926 Perman¹⁸ and Gold¹⁹ published roentgenograms and descriptions which brought forth for the first time the peculiarities evident in roentgenograms of vertebral hemangiomas. These were emphasized further in the excellent papers of Bailey and Bucy⁵ and Bucy and Capp²⁰. They found the picture one of irregular absorption of bony trabeculae and thickening of the remaining vertical trabeculae with resulting parallel vertical striations in the bodies of the vertebrae and loss of the normal homogeneous bony structure. Not uncommonly these abnormal trabeculations extended into the vertebral arches and laminae and involved more than one body. Because of the superimposed sternum, heart and mediastinal structures, the anteroposterior view fails to show the osseous changes as well as does the lateral view, which usually is diagnostic.

In 1929 Bailey and Bucy⁵ collected 10 cases of cavernous hemangioma of the vertebrae producing symptoms of compression myelitis and added 1 of their own. Laminectomy was performed in 5 of these, with death from shock and hemorrhage in the cases observed by Gold, Elsberg (cited by Globus and Doshay⁸) and Guillain, Decourt and Bertrand²¹. Recovery resulted from the procedure in the cases observed by Perman¹⁸ and by Bailey and Bucy,⁵ although in both cases the patient's condition became critical because of shock and hemorrhage. It seems obvious, therefore, that laminectomy in these cases is a dangerous procedure, and preparation for the treatment of shock and hemorrhage is necessary. It is not unlikely that some of the deaths previously reported as following laminectomy were the result of unnecessarily enthusiastic surgical efforts. Not only does any attempt to open the dura seem unwise in these cases, but any effort to obtain complete removal of an underlying epidural hemangioma is ordinarily as futile as it is unreasonable.

The use of roentgen therapy alone in cases of compression myelitis seems not only inadequate but hazardous, for irreparable damage to the

17 Hitzrot, J. M. Hemangioma Cavernosum of Bone, *Ann Surg* **65** 176 (April) 1917

18 Perman, E. On Haemangiomata in the Spinal Column, *Acta chir Scand* **61** 91, 1926

19 Gold, E. Von den Wirbelveränderungen im Falle eines Hemangioms der Dura spinalis, *Arch f klin Chir* **139** 729 1926

20 Bucy, P. C., and Capp, C. S. Primary Hemangioma of Bone with Special Reference to Roentgenologic Diagnosis, *Am J Roentgenol* **23** 1 (Jan) 1927

21 Guillain, G., Decourt, J., and Bertrand, I. Compression médullaire par angiome vertébral, *Ann de med* **23** 5 (Jan) 1928

cord may occur before any beneficial effect can be anticipated. So far it has not been tried sufficiently to enable one to determine whether it would be advisable during the early stages of compression should the diagnosis be made and the patient kept under observation. According to Bucy and Capp,²⁰ Perman's¹⁸ patient was in perfect health more than three years after laminectomy and postoperative roentgen therapy. Although the value of its use in these cases is uncertain, we believe that postoperative roentgen therapy is indicated and have given it to the patient in the present case, whose subsequent course will be followed with interest.

SUMMARY AND CONCLUSIONS

Hemangiomas of the vertebral column are not so much a pathologic as a clinical rarity. The present case is the twelfth in which such a condition caused compression myelitis, the first in which it was diagnosed preoperatively and the third in which it was successfully treated by operation. It is also one of the exceptional cases of vertebral hemangiomas associated with epidural hemangioma, the eighteenth case of epidural hemangioma of the spinal cord reported, and the eleventh such case in which the patient was cured after a laminectomy. Peculiarly, it is also the fourth case of hemangiomatous nevus of the skin occurring in the same dorsal segments as the epidural hemangiomas.

Whether vertebral and epidural hemangiomas represent neoplasms or vascular malformations remains a question. They are different from hemangioblastomas, relatively benign, slow in growth and not metastatic. Most of the accumulating evidence suggests a congenital origin.

With segmental involvement of the central nervous system, cutaneous nevi are diagnostically important.

As has been emphasized by Bucy and others, roentgenograms of the vertebrae reveal diagnostic peculiarities when the bone is involved by hemangiomas, particularly parallel striations in the vertebral bodies and loss of the normal homogeneous bony structure.

The high percentage of deaths following laminectomy in these cases shows that the procedure is a hazardous one, and preparations for the treatment of shock and hemorrhage should be made. It is suggested that the high mortality may have been the result of unnecessarily enthusiastic surgical efforts.

Although high voltage roentgen ray therapy is recommended as a postoperative measure, it would seem inadequate and hazardous to use such treatment alone when there is compression myelitis, for irreparable damage to the cord may occur before any beneficial effect can be anticipated.

PROTRUDED INTERVERTEBRAL DISK

REPORT OF A CASE, NOTE ON A POSSIBLE INFLAMMATORY
ETIOLOGIC FACTOR (CIRCUMSCRIBED ARACHNOIDITIS)

GILBERT C ANDERSON, M D

AND

ERWIN WEXBERG, M D

NEW ORLEANS

Protrusion of the intervertebral disk as the result of trauma was first mentioned by Virchow¹ in 1857, though it was not until more than fifty years later that Goldthwaite² pointed out its clinical significance. At almost the same time, Middleton and Teacher,³ of Glasgow, Scotland reported the full postmortem observations in such a case and correlated the clinical symptoms with the pathologic changes revealed at necropsy.⁴ Since then numerous cases have been reported in the literature, and the various aspects of the condition have been thoroughly discussed. The latest and one of the most extensive of these reports is an analysis by Love and Walsh⁵ of 100 cases in which operation was performed at the Mayo Clinic.

Since protrusion of the intervertebral disk is no longer regarded as rare or even as very unusual, the report of a single case demands some

From the Departments of Surgery and Neuropsychiatry of the School of Medicine of Louisiana State University and from the Charity Hospital of Louisiana at New Orleans

1 Virchow, R L K Untersuchungen über die Entwicklung des Schädelfundamentes im gesunden und krankhaften Zustande und über den Einfluss derselben auf Schädelform, Gesichtsbildung und Gehirnbau, Berlin, G Reimer, 1857

2 Goldthwaite, J E The Lumbo-Sacral Articulation An Explanation of Many Cases of "Lumbago," "Sciatica," and Paraplegia, Boston M & S J 164 365 1911

3 Middleton, G S, and Teacher, J H Injury of the Spinal Cord Due to Rupture of an Intervertebral Disk During Muscular Effort, Glasgow M J 76 1, 1911

4 W E Dandy (Loose Cartilage from Intervertebral Disk Simulating Tumor of Spinal Cord, Arch Surg 19 660 [Oct] 1929) reported 2 cases of "loose cartilage from intervertebral disk," the first cases of this kind in which the cartilage was detected at operation when tumors of the vertebrae were suspected. Sequestration of the protruded mass of cartilage obviously represents an advanced stage of simple protrusion, which is the more frequent finding.

5 Love, J G, and Walsh, M N Protruded Intervertebral Disk, Report of One Hundred Cases in Which Operation Was Performed, J A M A 111 2 (July 30) 1938

explanation. The justification is that this special case brings out clearly a point to which no great attention has been paid, namely, the possibility that an associated inflammatory process rather than protrusion of the disk per se may be responsible for the clinical symptoms.

REPORT OF A CASE

J. L., a white laborer 42 years old, was admitted to the Charity Hospital on April 27, 1938, complaining of dysuria and of pain in both legs. He had been entirely well until two months before admission, when he lifted a sack of sugar weighing about 200 pounds (90 Kg.) and was aware as he did so that he had twisted his body. Immediately he felt a sharp, shooting pain in his back, which some hours later radiated down the posterior aspect first of the right and later of the left lower extremity. Lifting such weights was part of his work and had never before caused any discomfort or pain.

The pains described recurred at irregular intervals without change in their character until he was admitted to the hospital. Weakness soon developed in both legs, and standing became impossible. Two weeks before he entered the hospital he had difficulty in urination, and the act finally became impossible without straining. Function of the bowel was not disturbed, but a few days after the urinary symptoms developed he noticed loss of sensation about the anus.

The previous history was without incident except for an appendectomy in 1927. There was no history of venereal infection. The patient said that he smoked moderately but rarely touched alcohol.

Physical examination revealed no deviation from the normal except for slight dyspnea and mild edema of both ankles. Neurologic examination also gave entirely negative results except for the following findings in the lower extremities.

All passive movements were normal, and the hip and knee joints could be moved normally on both sides. The strength of the right extremity was markedly and that of the left moderately reduced. The patient could stand and walk only if strongly supported. Coordination was normal. There was hypesthesia for all qualities in the left perianal area and on the left side of the genitalia (segments S₄ and S₅). There was no tenderness of the nerve points. Lasegue's sign was absent. The patellar reflexes were positive (2 plus) and equal. The achilles reflex was absent on both sides. The plantar reflex was positive and equal on both sides. Babinski's and Oppenheim's signs were absent.

Spinal puncture between the third and the fourth lumbar vertebra yielded clear fluid under 1 mm. of pressure, which rose to 3 mm. when the jugular veins were compressed. The reaction for globulin was plus 4 and each cubic millimeter contained 200 cells. The mastic curve was 0012333330. The Wassermann reaction was negative, and urinalysis showed no abnormalities.

Roentgen examination of the pelvis and of the lumbar portion of the spine showed no evidence of bony erosion. The bodies of the lower lumbar vertebrae showed hypertrophic changes. Twenty-five days after admission, myelographic examination after injection of iodized poppyseed oil into the cisterna showed that the oil was apparently arrested at the midportion of the third lumbar vertebra, all of it had not gravitated to this level. Anteroposterior and lateral views of the lumbar portion of the spine taken on the next day showed the oil still arrested at this point. No characteristic deformity could be made out in any of the pictures. A diagnosis was made of a possible tumor of the cauda equina at the level of the third lumbar vertebra and laminectomy was advised.

Operation (by G C A) was done thirty-six days after admission with the patient under general anesthesia. The spines and laminae of the second and of the third lumbar vertebra were removed. The exposed dura looked normal, but no pulsation was visible until the spine and lamina of the first lumbar vertebra had been removed, then pulsation was noted in the upper angle of the space. When the dura was opened, spinal fluid and iodized oil promptly gushed out. No tumor or obstruction could be seen, and a grooved director passed 5 inches (12.5 cm) up the canal without encountering any resistance. When the strands of the cauda equina were separated, a slight protrusion of the intervertebral disk could be detected at the lower portion of the wound, probably the fourth lumbar vertebra. The protrusion was so slight that it seemed entirely insufficient to account for the severe clinical symptoms. It was removed with a curet after the dura had been split anteriorly. The dura was closed posteriorly with silk, and the wound was sutured in layers about a rubber dam drain.

The postoperative diagnosis was herniation of the fourth lumbar intervertebral disk.

For five days after the operation the patient complained of pains in his legs, by the eighth day the pains had entirely disappeared. At this time he complained of some numbness in the right foot. On the twelfth day he complained of pain in the left buttock and down the flexor surface of the left thigh. There was no pain on the right side. Movements in the left hip and knee joints were slightly weaker than in the right. On the left, plantar flexion of the ankle joint was of almost normal strength, and dorsal flexion and pronation, though still weak, were normal in extent. On both sides movement of the toes was normal and the patellar reflexes were positive and equal, but the achilles reflex was absent. There were no sensory disturbances. At no time was there any motor weakness or anesthesia or any lack of control of the bladder and the anal sphincters, though there was some frequency of urination. The dysuria complained of before operation had entirely disappeared.

The patient was discharged on the twelfth postoperative day, with all his symptoms markedly improved and with every indication that recovery would be complete. In spite of repeated requests he has failed to return for a follow up study.

The excised specimen was reported microscopically as a portion of fibrous cartilage with calcification.

COMMENT

In spite of the rather extensive literature which has arisen about protruded intervertebral disk, several phases of the condition are still far from clear. There is still not complete agreement, for one thing, as to exactly what the pathologic process is. Schmorl and Junghans,⁶ who described the protrusion as a "nodule," and Andrae,⁷ who spoke of it as *Knorpelknötchen*, stated the belief that the pathologic change is primarily prolapse of the disk secondary to a tear in the annulus fibrosus.

6 Schmorl, G, and Junghans, H. Die gesunde und kranke Wirbelsäule im Röntgenbild, Leipzig, Georg Thieme, 1932.

7 Andrae, R. Ueber Knorpelknötchen am hinteren Ende der Wirbelsäule. Mittheilungen aus dem Anatomischen Institut der Universität zu Leipzig, 1929.

Slaughter⁸ expressed the same opinion. Alpers, Grant and Yaskin⁹ pointed out that in their cases the herniated mass consisted microscopically of fibrocartilage, which is histologically very different from the nucleus pulposus. Minter and Ayer¹⁰ found both nucleus pulposus and annulus fibrosus in their specimens.

There is also some discussion as to whether the protruding mass should not be considered a neoplasm. The data in 1 of the cases reported by Alpers, Grant and Yaskin⁹ and in another, reported by Bucy,¹¹ furnish histologic evidence to this effect. Elsberg¹² took an intermediate position suggesting that the protruding mass is not a true neoplasm but a form of local hyperplasia of the cartilage, which can be described as ecchondrosis. The findings in our own case suggest the same interpretation.

The case which we have reported is like most other cases in that the etiologic factor was traumatic. On the other hand Stookey,¹³ Elsberg¹² and Bucy,¹¹ in most of whose cases localization of the pathologic process was in the cervical portion of the spine, stated the opinion that trauma is a rare cause and advocated a neoplastic hypothesis. Minter and Ayer¹⁰, Love and Walsh,⁵ Hampton and Robinson¹⁴ and Simonds¹⁵ in most of whose cases localization was in the lumbar portion of the spine, usually between the fourth and the fifth lumbar vertebra concluded that trauma is a very important cause. Love and Walsh⁵ in discussing this point, noted that the condition in the greatest number of cases occurs in the area of the greatest convexities of the spine, which in heavy lifting or pushing bear the greatest mechanical strain. These

8 Slaughter, R. F. Herniation or Rupture of Intervertebral Disc. Report of Two Cases, *South M J* **30** 803, 1937.

9 Alpers, B. J., Grant, F. C., and Yaskin, J. C. Chondroma of the Intervertebral Disks, *Ann Surg* **97** 10, 1933.

10 Minter, W. J., and Ayer, J. B. Herniation or Rupture of the Intervertebral Disk into Spinal Canal, *New England J Med* **213** 385, 1935.

11 Bucy, P. C. Chondroma of Intervertebral Disk, *J A M A* **94** 1552 (May 17) 1930.

12 Elsberg, C. A. Extradural Spinal Tumors. Primary, Secondary, Metastatic, Surg., Gynec. & Obst. **46** 1, 1928. The Extradural Ventral Chondromas (Ecchondroses). Their Favorite Sites, Spinal Cord and Root Symptoms They Produce, and Their Surgical Treatment, *Bull Neurol Inst New York* **1** 350, 1931.

13 Stookey, B. Compression of the Spinal Cord Due to Ventral Extradural Cervical Chondromas. Diagnosis and Surgical Treatment, *Arch Neurol & Psychiat* **20** 275 (Aug.) 1928.

14 Hampton, A. O. and Robinson, I. M. The Roentgenographic Demonstration of Rupture of Intervertebral Disk into the Spinal Canal After the Injection of Lipiodol with Special Reference to Unilateral Lumbar Lesions Accompanied by Low Back Pain with "Sciatric" Radiation, *Am J Roentgenol* **36** 782, 1936.

15 Simonds, F. L. Low Back Pain Due to Herniation or Rupture of Intervertebral Disk into Spinal Canal. *Nebraska M J* **22** 456, 1937.

facts obviously fit better with the conception of herniation than with that of neoplasm. The condition in Dandy's¹⁶ 2 cases, in which loose cartilage instead of herniated tissue was found, was probably due to a traumatic mechanism.

The calcification observed in our specimen fits into the picture of trauma, for calcification in traumatized cartilage is not altogether rare. Schmorl and Junghans⁶ made the statement that posterior ruptures of the nucleus pulposus may be associated with calcification, but Hampton and Robinson,¹⁴ who observed calcification in only 1 of 39 cases studied, concluded that this process was not true calcification but a fragment of fractured vertebra. In view of the differing reports in the literature it seems reasonable to question whether the condition is similar either etiologically or pathologically in all cases.

As all reports have pointed out, the clinical symptoms of protrusion of an intervertebral disk are most often those of persistent lumbago or sciatica which makes its appearance immediately after a strain or injury and which does not respond to any of the usual methods of treatment. In some cases symptoms are delayed, and in others, as in 29 of the 100 reported by Love and Walsh,⁵ no history of trauma can be obtained. Echols¹⁷ recently called attention to the importance of suspecting this condition in cases of supposed sciatica which does not respond to the usual measures and has outlined the mechanism by which the pain is produced.

Visualization of the spinal canal by injection of iodized poppyseed oil should always be employed. It usually shows a ventral filling defect and only rarely a complete block, as in our case and in the cases reported by Slaughter,⁸ Capener,¹⁸ Simonds,¹⁵ Mixter and Ayer¹⁰ and Hampton and Robinson.¹⁴

In the cases reported by Flothow,¹⁹ Mixter and Ayer¹⁰ and Hampton and Robinson,¹⁴ as well as in our own, there was evidence of a lesion of the cauda equina with the pain syndrome, manifested by loss of the achilles reflexes, hyperesthesia of the sacral segments, sphincteric disturbances and more or less marked motor weakness. That the pain is due to compression by the protruding disk of the nerve root as it emerges from the dural canal is an entirely satisfactory explanation in those cases in which lumbago or sciatic pain is the only clinical symptom. It is not, however, a satisfactory explanation in cases in which the

¹⁶ Dandy, cited in footnote 4.

¹⁷ Echols, D. H. Ruptured Intervertebral Disk. A Cause of Sciatic Pain. *New Orleans M. & S. J.* **91** 243, 1938.

¹⁸ Capener, N. Intractable Sciatica Due to Prolapsed Intervertebral Disk Treated by Laminectomy, *Proc. Roy. Soc. Med.* **30** 1262, 1937.

¹⁹ Flothow, P. G. Nucleus Pulposus and Hypertrophy of the Ligamentum Flavum, *Northwest Med.* **37** 14, 1938.

protruding cartilage is very small and the neurologic lesion is extensive. This disproportion existed in our case in which the size of the protrusion was even less than the 0.75 to 1 cm. mentioned by Naffziger, Inman and Saunders²⁰ and others. In such severe involvement there is evidently compression of the entire dural canal, which cannot be accounted for merely by the pressure of the protruding cartilage.

In our personal case and in such similar ones as those reported by Hampton and Robinson¹⁴ and by Slaughter⁸ a more complex pathogenic mechanism is evidently responsible. In our opinion this mechanism is inflammatory. The unusually high number of cells (200 per cubic millimeter) in the spinal fluid in our case seems to point definitely to an inflammatory process which, we believe, is local circumscribed arachnoiditis provoked by mechanical irritation from the protruding disk. A consideration of the operative findings supports this point of view. After the subarachnoid space was opened, spinal fluid gushed out, and pulsation soon became apparent for the first time. There were no macroscopic local changes in the meninges, and our idea is that with the dura an arachnoiditic cyst was opened, which contained spinal fluid, increased by some exudate, under considerable pressure. Such a cyst could easily account both for the blockage of the canal which was noted in successive roentgenograms and for the compression of the cord which caused the severe clinical symptoms. The very low pressure found at spinal puncture before operation is accounted for by the fact that the puncture was made between the third and the fourth lumbar vertebra, that is, below the arachnoiditic cyst. The high globulin content of the spinal fluid is also evidence of the chemical changes which are to be expected in association with compression.

It has long been known that circumscribed meningitis, of whatever origin, may produce all the symptoms of a tumor of the spinal cord. Thorburn,²¹ in 1918, said "The writer has operated upon at least one case in which careful exploration for a tumor of the cauda equina, of which the symptoms were regarded as unequivocal, revealed no growth, but in which the theca presented distinct thickening and contained much fluid, while complete recovery ensued." In a case in which a diagnosis of protrusion of the intervertebral disk had been made, Peet and Echols²²

20 Naffziger, H. C., Inman, V., and Saunders, J. B. Lesions of Intervertebral Disc and Ligamenta Flava. *Clinical and Anatomical Studies*, Surg., Gynec. & Obst. **66** 288, 1938.

21 Thorburn, W. Operations upon the Spinal Cord and Canal, in Burghard, F. F., and Kanel, A. B. *Oxford Surgery*, New York, Oxford University Press, 1918, sect. 5, pt. 2, p. 416.

22 Peet, M. M., and Echols, D. H. Herniation of the Nucleus Pulposus. A Cause of Compression of the Spinal Cord, *Arch. Neurol. & Psychiat.* **32** 924 (Nov.) 1934.

found xanthochromia, 38 lymphocytes per cubic millimeter and a colloidal gold curve in which the maximum precipitation was shifted to the right. Thickening of the arachnoidea was established. In Slaughter's⁸ case there were 33 cells per cubic millimeter of spinal fluid and a midzone rise in the colloidal gold curve. In Capener's¹⁸ case the dura was opened and an apparent circumferential constriction found, but the projecting portion of the disk was not removed.

In view of these facts, the question arises whether cases of protruded intervertebral disk should not be divided into two groups:

- 1 Cases of lumbar or sacral radiculitis caused by pressure of a protruding intervertebral disk

- 2 Cases in which the symptoms are those of a lesion of the cauda equina and are due to circumscribed meningitis which has been provoked by the mechanical irritation of a protruding intervertebral disk

SUMMARY

A case is recorded in which protrusion of the fourth intervertebral disk, with consecutive circumscribed spinal meningitis, gave rise to symptoms simulating those of a tumor of the cauda equina. Incision of the meningitic cyst and excision of the small protruding disk initiated recovery.

This case and a few similar cases recorded in the literature suggest that a distinction is justified between (a) cases of lumbar or sciatic radiculitis caused by the pressure of a protruding intervertebral disk and (b) cases of compression of the cauda equina by a meningitic cyst which has developed from the mechanical irritation produced by the protrusion of an intervertebral disk.

STUDIES IN CROSS CIRCULATION

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In 1931 Firor¹ described a method for crossing the circulations of dogs by means of an end to end anastomosis (according to Carrel's technic) of the carotid artery of one dog and the jugular vein of another, and vice versa². No anticoagulant was required. Firor found this a reliable method for providing adequate mixing of the blood and made certain physiologic observations during the procedure. The methods which had been previously used were reviewed³ and attention was called to the fields of investigation in which these procedures had been employed. Recent studies involving the use of cross circulation⁴ have suggested the need for additional information concerning the accompanying physiologic changes, especially the alterations in plasma and blood volume, the changes in blood pressure and the influence of such changes on the blood volumes, and the rapidity and completeness of mixing of the blood.

MATERIAL AND METHOD

We have employed Firor's technic in our experiments and have found it reliable, relatively simple and not time consuming. The time required for operation was fifty to sixty minutes. Only one change has been instituted. In experiments of short duration it has proved easier to place the animals on the table so that their heads face in opposite directions. The wound may be left open and merely covered with a pledget of cotton moistened with warm physiologic solution of sodium chloride, a method which permits routine inspection at frequent intervals to make

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1 Firor, W. M. Experiments in Cross Circulation, *Am J Physiol* **96** 146-152, 1931.

2 In 1925 Ivy, Lim and McCarthy (*Am J Physiol* **74** 616-638, 1925) utilized actual anastomosis by suture in producing cross circulation. These authors, however, did carotid to carotid and carotid to carotid and also carotid to carotid and jugular to jugular anastomoses.

3 Firor, W. M. A Review of Cross Circulation Experiments, *New England J Med* **204** 157-159, 1931.

4 Firor, W. M., Lamont, A., and Shumacker, H. B., Jr. Studies on the Cause of Death in Tetanus, *Ann Surg*, to be published.

sure of the proper functioning of the anastomoses.⁵ The operations were done with the dogs under pentobarbital sodium anesthesia. In the study reported here normal healthy mongrel dogs were used except in experiments concerned with changes in temperature and the effect of muscular exercise on the blood sugar levels. In the latter instances cross circulation was produced between a normal dog and a dog having almost constant clonic convulsions of the hindlimbs consequent to the injection of tetanus toxin into the lumbar portion of the spinal cord.⁴

Samples of blood were collected in bottles containing dried potassium and ammonium oxalate.⁶ For hematocrit determinations the Wintrobe hematocrit tubes were used. Determinations of the values for blood sugar were done according to the Folin-Wu technic. The values for plasma proteins were determined by the falling drop method with the LaMotte densimeter. Mean arterial blood pressures were obtained by means of a cannula in the carotid artery connected with a mercury manometer, a small bulb filled with sodium citrate solution near the cannula being employed to prevent clotting.

The plasma volume of each dog was determined immediately after completion of the anastomoses and before cross circulation was begun (with the rubber-shod artery clamps still in place) and again immediately after the cross circulation was ended. The photoelectric microcolorimetric technic with the azo blue dye T 1824⁷ was used. Since the original plasma volumes and concentrations of proteins in the plasma were known, the plasma volume for each dog before the anastomoses were opened and the combined volume for both dogs during the period of cross circulation could be estimated from the plasma protein concentrations, the amount of plasma which had been withdrawn in blood sampling being taken into consideration. This method is accurate provided there has been no loss of proteins other than that due to bleeding, and there is good evidence that this is true and the method is valid. The question of loss of proteins could be checked accurately in those experiments in which no loss of blood was sustained when the anastomoses were opened at the beginning of the cross circulation. In these instances the values for total protein at the beginning of the experiment and at the end, calculated from the values for plasma volume obtained by the dye method and the protein concentration, checked within 2.5 per cent. In the other experiments in which it was necessary to include in the calculations an estimate of the amount of blood lost on opening the anastomoses the values for total protein at the beginning and at the end of the experiments generally checked within 1.5 per cent, and the discrepancy was never greater than 5 per cent.

RESULTS

Blood Pressure—In table 1 are recorded changes in blood pressure during cross circulation. It is apparent that there is, in general, a drop in pressure in both dogs shortly after cross circulation is begun. The drop is generally precipitous and considerable. After this initial fall there is a tendency for the pressure to rise toward its former level.

5 In longer experiments the animals should be placed head to head, the wound closed and the necks and forelegs strapped together with adhesive tape. The functioning of the anastomoses can be ascertained by detection of a bruit.

6 One and three-tenths grams of ammonium oxalate and 0.7 Gm of potassium oxalate in 100 cc, 0.1 cc for each each cubic centimeter of blood (Wintrobe).

7 Gibson, J. G., Jr., and Evelyn, K. A. *Clinical Studies of the Blood Volume*. IV. Adaptation of the Method to the Photoelectric Micro-Colorimeter, *J. Clin. Investigation* 17: 153-158, 1938.

TABLE 1—Changes in Blood Pressure During Cross Circulation

		Mean Arterial Blood Pressure, Mm. of Hg.															After	
Experiment No.	Dog	Original	Before															Anastomosis Was Closed
			Arterial Opened	2 Minutes After	5 Minutes After	10 Minutes After	10 Minutes After	15 Minutes After	30 Minutes After	60 Minutes After	80 Minutes After	100 Minutes After	120 Minutes After	135 Minutes After	200 Minutes After			
1	A	140	119	62	73	81	100	110	118	128	134	137	143	141	150 to 145			
	B	111	60	98	90	80	81	96	101	101	123	122	121	121	125 to 110			
2	A	118	161	115	60	60	71	75	75	70	68	60			50 to 101			
	B	118	60	115	160	160	118	111	112	110	114	110			15 to 115			
2	A	160	111		115	100	110	90	98	115	125	123			125 to 108			
	B	110	10		105	100	100	72	62	70	95	95			100 to 160			
4	A	178	161	91	20	65	72	61	60	72	82	85			95 to 118			
	B	150	80	172	60	72	93	102	120	160	170	170			141 to 110			
5	A	192	130	60	21	50	104	94	70	62	100	110			115 to 126			
	B	110	78	60	50	62	81	81	70	71	75	90			95 to 160			
8	A	164	125		140	124	70	122	170	132	130	171			122 to 72			
	B	168	162		141	110	83	112	118	108	103	94			105 to 118			
10	A	162	152		150	128	141	142	130	121	120	112	116		122 to 108			
	B	150	146		98	100	132	132	132	118	100	180	178		178 to 161			
11	A	190	172	122		100	90	170	140	145	118	170			150 to 105			
	B	105	150	113		116	103	150	148	158	150	165			108 to 110			

After the cross circulation is ended the pressures usually rise. There is no correlation between the original blood pressure and that observed during the cross circulation.

Plasma and Total Blood Volume—We have tabulated the essential data in table 2 and have charted 3 illustrative experiments (charts 1, 2 and 3). Our chief concern has been the question of blood shift from one animal to the other during the cross circulation. The results in

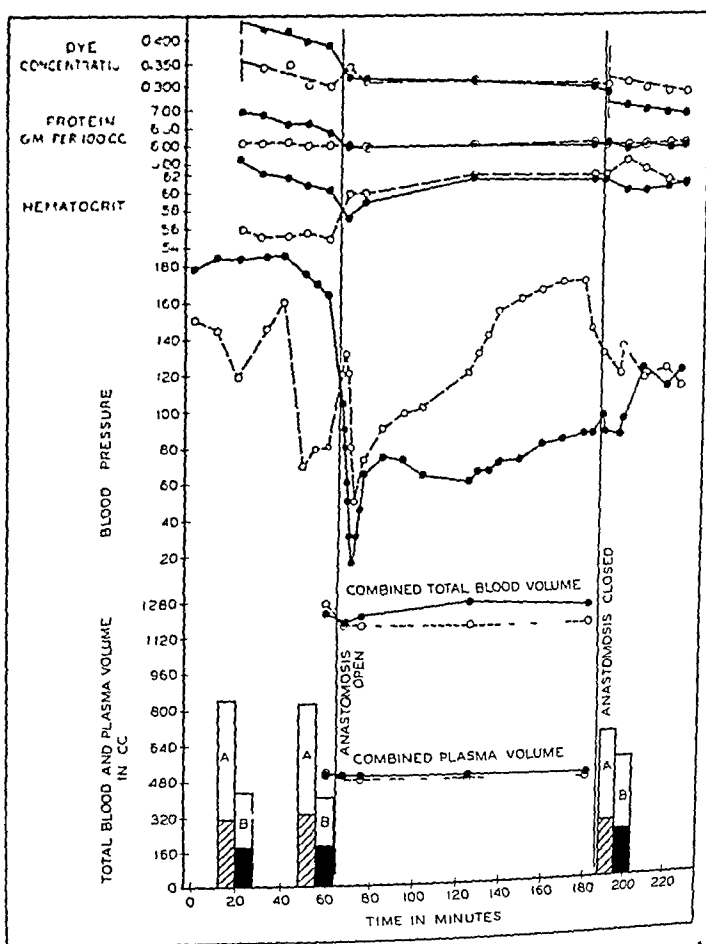


Chart 1 (experiment 4)—Loss of blood from dog A (the larger dog) to dog B (the smaller dog). The difference in the blood pressures during cross circulation is to be noted. In this, as well as in charts 2 and 3, the promptness and adequacy of the mixing of dye, proteins and red cells is illustrated, also the increase in the total blood volume during cross circulation. In charts 1, 2 and 3 the values for dog A are charted as unbroken lines and solid circles and those for dog B as broken lines and open circles. Likewise, in all three charts the solid lines accompanying the words "combined total blood volume" and "combined plasma volume" represent the actual calculated values, and the dotted lines represent the estimated values obtained by deducting from the original values the amounts withdrawn. The cross-hatched and solid portions of the columns represent the plasma volume, the total height of the columns, the total blood volume. The optical density is charted as dye concentration.

table 2 are expressed in the number of cubic centimeters of difference between the calculated and the actual volume after the cross circulation

The final values for blood and plasma volume cannot be safely estimated by simply deducting the volume withdrawn for examination and adding the volume of dye solution introduced during the procedure for there are increases and decreases in blood and plasma volume out of proportion to the amount of fluid withdrawn or added. For example, although 20 cc of blood was drawn and from 13 to 20 cc of fluid added during the forty minutes between the original

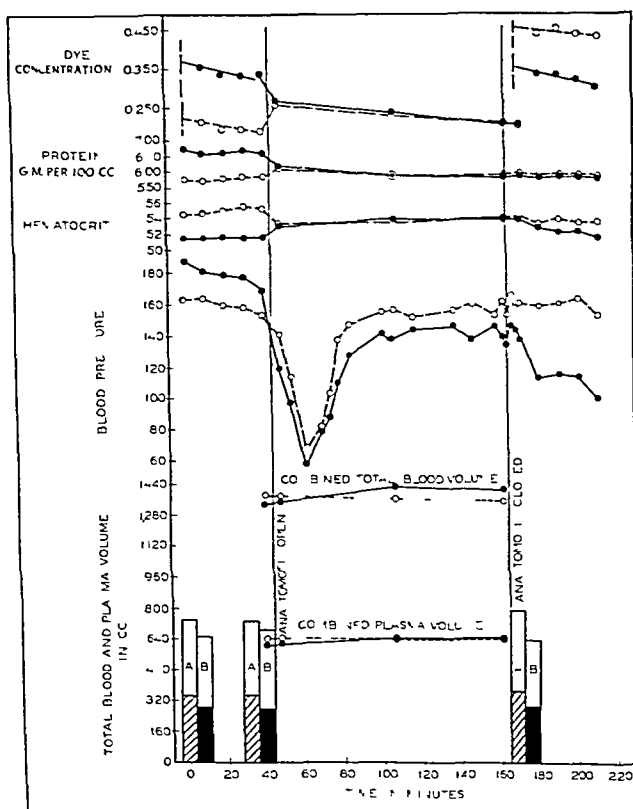


Chart 2 (experiment 11)—Chart showing no relative change in total blood and plasma volume during cross circulation in two dogs of nearly equal size. The blood pressures of the dogs do not differ greatly during cross circulation.

determinations of volume and those recorded just before the anastomoses were opened, there were changes in plasma volume as great as ± 46 and -26 cc and in total blood volume as great as ± 133 and -66 cc. Furthermore, the difference between the actual calculated combined plasma volumes toward the end of cross circulation and the values estimated by subtraction of the removed fluids from the sum of the initial values for plasma volume varied from $+44$ to -20 cc while the difference between the actual calculated and the estimated total values for blood volume varied from ± 203 to -25 cc. Consequently, in calculating the final values which might be expected if no shift had taken place, we have assumed that

the combined plasma and total blood volumes just before the cross circulation was ended would be distributed between the two dogs in the same proportion that existed just before cross circulation was begun. Though not entirely accurate, since further changes may take place during a few minutes before reinjection of the dye this is a reasonably good method of calculating what the final values would be if there were no loss of blood from 1 dog to the other.

The preceding discussion, furthermore, makes evident two other points. The plasma volume varies decidedly less than does the total red

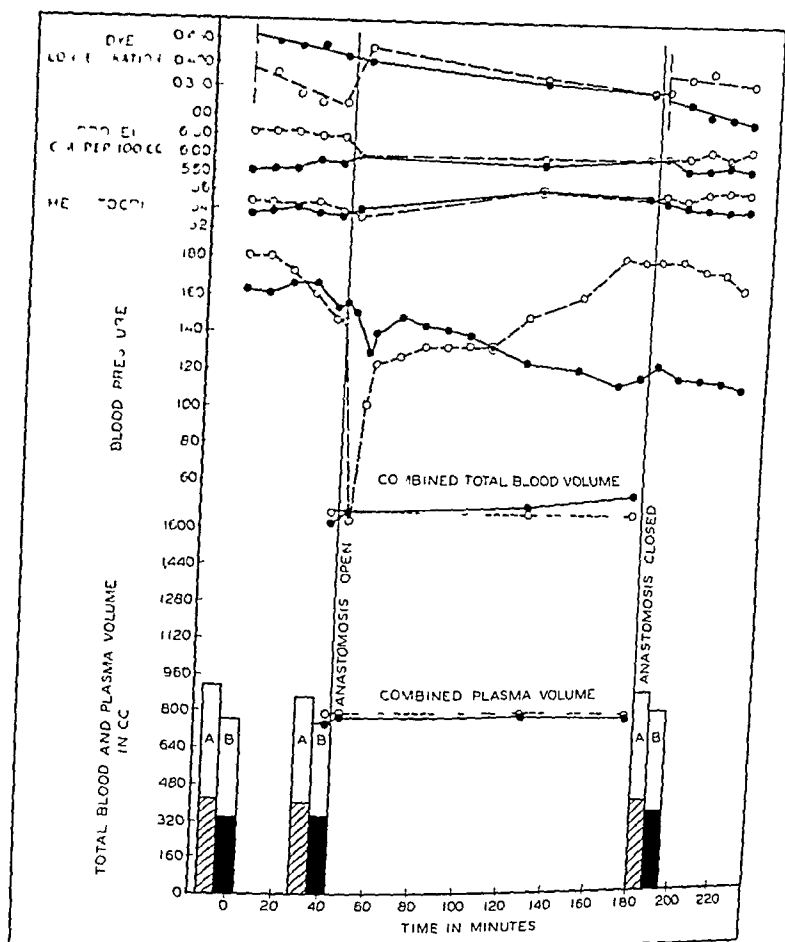


Chart 3 (experiment 10) —Chart illustrating the fact that blood pressures may differ considerably without causing a loss of blood from one animal to the other

cell volume and consequently varies less than the total blood volume, hence determinations of the plasma volume are more reliable than determinations of the total blood volume as far as estimation of blood shift is concerned. Only fairly great changes can be considered significant evidence of shift of blood from one animal to the other, because the values vary widely even when there has been no stimulus other than the withdrawal or addition of a few cubic centimeters of fluid.

TABLE 2—*Studies of the Blood and Plasma Volume During Cross Circulation*

Experiment No	Dog	Total Blood Volume, Cc				Plasma Volume, Cc				Duration of Cross Circulation, Hours	Weight of Dog, Kg.	Blood Pressure During Cross Circulation
		Original	Just Before Anastomosis Was Opened	Infus. I	Difference Between Calculated and Actual Volumes	Original	Just Before Anastomosis Was Opened	Infus. I	Difference Between Calculated and Actual Volumes			
1	A B	593 510	475 407	426 112	9 -22	253 212	250 211	221 216	-9 12	3.5	5.20 4.55	62 118 177 141 98 101 122 121
2	A B	1131 402	1080 521	811 530	-218 187	525 225	499 221	61 280	-10 167	2	10.10 4.90	60 75 60 100 112 160
3	A B	785 561	918 501	707 176	-68 13	380 283	420 270	331 227	-19 -22	2	9.00 5.50	117 93 126 103 62 95
4	A B	811 112	819 407	660 553	-165 1129	307 190	320 183	246 213	-50 111	2	6.80 4.90	20 60 82 60 120 170
5	A B	615 161	625 490	551 189	-90 135	310 210	313 212	278 215	-37 111	2	7.60 5.20	24 101 62 100 50 81 71 75
8	A B	404 527	180 525	509	-14	200 213	216 218	214	13	2	7.73 7.72	110 170 170 154 118 108
10	A B	915 768	875 717	870 719	-15 9	425 318	400 311	401 311	-9 3	2.25	10.70 8.10	160 112 120 23 132 160
11	A B	750 651	738 626	708 670	115 -13	350 291	354 268	376 291	111 -5	2	7.10 6.20	100 110 118 116 158 160

In the 8 experiments which we carried out a considerable shift of blood occurred in 1 (experiment 2) and a fairly definite shift in another (experiment 4). In both instances there was a pronounced difference between the original blood and plasma volumes for the two dogs, and in both the larger dog lost blood to the smaller. In both experiments there was a great difference between the blood pressures of the two dogs during the period of cross circulation, and in both the loss of blood was suffered by the dog with the lower pressure. The details of experiment 4 may be seen in chart 1. In a third experiment (experiment 3) in which there was a wide difference between the original blood and plasma volumes of the two dogs there was no loss of blood from one animal to the other. A slight shift did occur in experiment 5. In this experiment there was a moderate difference in the original blood and plasma volumes of the two animals and very little difference between the blood pressures, and again the loss of blood was from the larger dog to the smaller. In none of these experiments was the loss of blood sufficient to cause the death of the animal. In the remaining experiments, in which the original blood and plasma volumes of the two dogs varied less, there was no apparent loss of blood from one animal to the other. Chart 2 represents experiment 11, in which the blood pressures varied little, chart 3 represents experiment 10, in which during the last hour of cross circulation there was a significant difference between the blood pressures of the two dogs.

In every instance except 1 (experiment 1) there was an apparent increase in the combined total blood volumes during cross circulation. This was largely due to an increase in the total red cell volume as there was either no increase or very little increase in the plasma volume during this period. These changes may be seen in charts 1, 2 and 3.

Mixing of Formed and Chemical Elements of the Blood—In table 3 are recorded changes in the volume of packed red cells during cross circulation, and in table 4, changes in the level of plasma proteins. It is evident that the values for the two dogs tended to become approximately equal within a few minutes after cross circulation was begun and to remain approximately equal during the experiment. The same holds true for the concentration of the azo blue dye, as may be seen in the 3 experiments charted.

The question arose whether if any chemical substance were utilized by one animal more rapidly than by the other or were supplied to one animal in greater quantity than to the other the values for this substance would be unequal in the 2 animals. In order to test this question the following experiments were done. First, to one of a pair of normal dogs between which adequate cross circulation had been established a slow intravenous drip of 50 per cent dextrose solution was given over

TABLE 3—Hematocrit Studies During Cross Circulation

Experiment No	Dog	Orig. Inly	Just Before Anastomosis Was Opened	Volume per Cent of Packed Red Cells										After Anastomosis Was Closed	
				2½ Minutes After	3 Minutes After	10 Minutes After	15 Minutes After	20 Minutes After	25 Minutes After	45 Minutes After	60 Minutes After	120 Minutes After	180 Minutes After		450 Minutes After
1	A B	40.7 52.5	45.5 51.5												18.2 48.0
2	A B	53.7 54.7	53.8 57.0			55.0 55.8	54.5 54.8	53.5 55.0	54.0 53.8			58.0 57.0		55.8 55.2	
3	A B	51.6 40.5	53.6 51.0			51.2 51.3	51.0 51.2			51.7 52.0		52.1 51.0		53.2 52.1	
4	A B	57.5 50.0	50.2 54.0	57.1 59.8		53.0 60.0					61.1 61.0	61.2 61.5		61.2 61.1	
5	A B	51.2 47.9	50.1 46.0		48.2 40.0	40.8 48.1				10.6 10.8		19.6 19.0		19.8 19.8	
7	A B	55.0 50.0			53.4 53.2						55.0 55.0	52.6 53.2			
8	A B	57.7 50.6	55.0 52.8			54.5 54.5					54.0 54.5	53.2 53.0		53.0 53.0	
9	A B	54.5 60.0	54.2 60.0		54.6 54.4						59.1 59.2	58.0 58.3		61.5 61.5	
10	A B	53.6 54.8	53.2 53.8		54.0 53.2						56.2 56.2	55.8 55.0		55.0 55.8	
11	A B	51.8 46.8	52.0 43.0	53.4 53.0							54.3 54.0	54.2 54.1		54.1 54.8	
15	A B	40.0 42.0												52.0 51.0	

TABLE 4—*Studies of the Plasma Protein During Cross Circulation*

Experiment No	Dog	Originally	Just Before Anastomosis Was Opened	Plasma Protein, Gm per 100 Cc										180 Minutes After	After Anastomosis Was Closed
				2 1/2 Minutes After	5 Minutes After	10 Minutes After	15 Minutes After	20 Minutes After	25 Minutes After	45 Minutes After	60 Minutes After	120 Minutes After			
1	A	5.00	4.65												
	B	4.50	4.30												
2	A	6.86	7.10												
	B	6.86	6.69												
3	A	6.53	5.72			6.65	6.55	6.73							
	B	5.51	5.51			6.94	6.94	6.76	6.55						
4	A	6.93	6.38			5.65	5.51			5.51				6.73	
	B	6.10	6.04	5.97		5.51	5.39			5.17				7.15	
5	A	5.94	5.70			5.97								5.51	
	B	5.64	5.60			5.97								5.23	
8	A	6.10	5.65		5.66	5.22					5.97	5.97		6.04	
	B	6.27	6.23		5.25	5.20				4.95				5.97	
9	A	6.50	6.16			5.70						4.98		5.22	
	B	6.10	6.03			5.94				5.22		4.95		4.95	
10	A	5.52	5.50		6.00						5.45	5.76		6.00	
	B	6.63	6.43		5.79						5.70	5.90		5.94	
11	A	6.75	6.75		5.96						5.78	5.63		5.65	
	B	5.76	5.90	6.24	5.96						5.75	5.66		5.67	
				6.22							5.72	5.90		5.90	
											5.95	5.95		5.98	
														6.02	

a period of an hour and three quarters at the rate of about 17 cc per minute. The result is shown in chart 4. The animal receiving the intusion maintained a higher blood sugar level than did the other the difference varying from 10 to 91 mg per hundred cubic centimeters. In other experiments, in which cross circulation was established between a normal dog and a dog in active convulsions from induced tetanus (table 5), the blood sugar level of the dog undergoing violent exercise consistently remained much lower than that of the normal dog.

Pulse, Respiration and Temperature—The differences which others have noted¹ in the pulse rates and respiratory rates of two animals during cross circulation were confirmed by our studies. Others¹ also

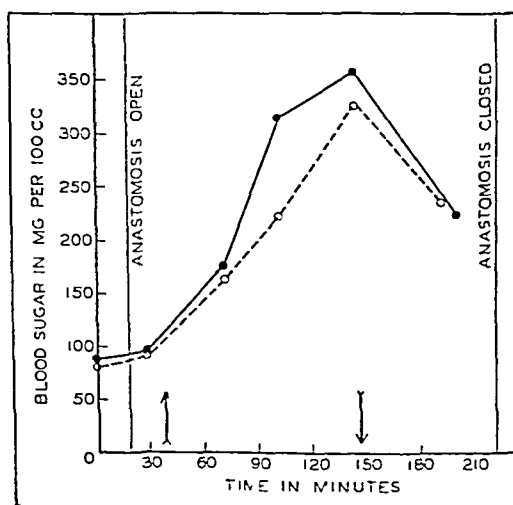


Chart 4 (experiment 6)—Chart showing values for blood sugar in 2 dogs during cross circulation, one of which is given an intravenous drip of dextrose solution. The arrows indicate the points at which the infusion in dog A (unbroken line) was begun and ended.

have found that the temperatures of animals during cross circulation may be different. We have made no studies of the temperature during cross circulation with normal animals, but we have made observations in about 40 experiments in which cross circulation has been established between a normal dog and a dog with tetanus. In these experiments (chart 5) the temperature of the normal dog rises with that of the dog with tetanus though it remains usually a degree or so lower. The temperature of the dog with tetanus is not proportionately reduced but is on the other hand, just about what it would be if cross circulation had not been carried out.

COMMENT

FIROR's technic for cross circulation is a reliable method for providing prompt and adequate mixing of the bloods of two animals. It is relatively simple and requires no elaborate equipment. The volume of packed red cells, the plasma proteins and the concentration of the dye become approximately equal in the two dogs within a few minutes after cross circulation is begun. Firor¹ has likewise shown that the values for chlorides, phosphates and sugar are equal during cross circulation. If one element of the blood, for example, sugar, is supplied continuously in greater amount to or is utilized more rapidly by one dog than by the other, the concentrations will not be equal. The

TABLE 5—*Effect of the Convulsions of Tetanus on Blood Sugar During Cross Circulation*^{*}

Experiment No	Subject	Blood Sugar, Mg /100 Cc					Therapy
		Before Cross Circulation	2 Hours After	4 Hours After	5 Hours After	21 Hours After	
12	Dog with tetanus	53		65			None
	Normal dog	95		96			None
13	Dog with tetanus	43	47		45		None
	Normal dog	90	89		102		None
14	Dog with tetanus	48				48	85 Gm dextrose by vein from 1 to 15 hours after cross circulation was begun
	Normal dog	88				93	25 Gm dextrose by vein 4 hours after cross circulation was begun 280 cc saturated dextrose solution by mouth from 1 to 2 hours before last blood sugar determination

* One dog in each experiment had severe convulsive movements of the hindlimbs consequent to the injection of tetanus toxin into the lumbar portion of the spinal cord.

temperature of a normal dog rises when cross circulation is established between it and a dog with an experimentally induced fever (tetanus). Pulse and respiration do not follow the same rate in both animals. The blood pressures of the two animals may differ widely. There is a tendency for an abrupt and relatively great fall in pressure to take place shortly after cross circulation is begun and for a gradual rise toward the normal level to occur thereafter. The drop is probably due to the sudden decrease in the peripheral resistance associated with opening of the arteriovenous fistula. The blood pressures during cross circulation do not bear any constant relation to the preoperative pressures. There is generally an absolute increase in total blood volume during cross circulation, effected almost entirely through an increase in the total circulating red cell volume.

With dogs of roughly equal weight and consequently with approximately equal blood and plasma volume there is apparently no danger of net loss of blood from one animal to the other, even though there may be moderately great differences in the mean arterial blood pressures during the procedure. When the original blood and plasma volumes of the two dogs are very different there may occur a net loss of blood from the larger dog to the smaller, though this does not invariably take place. This can occur when the larger animal has a blood pressure much lower than that of the smaller. The lower arterial blood pressures in these experiments may be the result of loss of blood rather than one

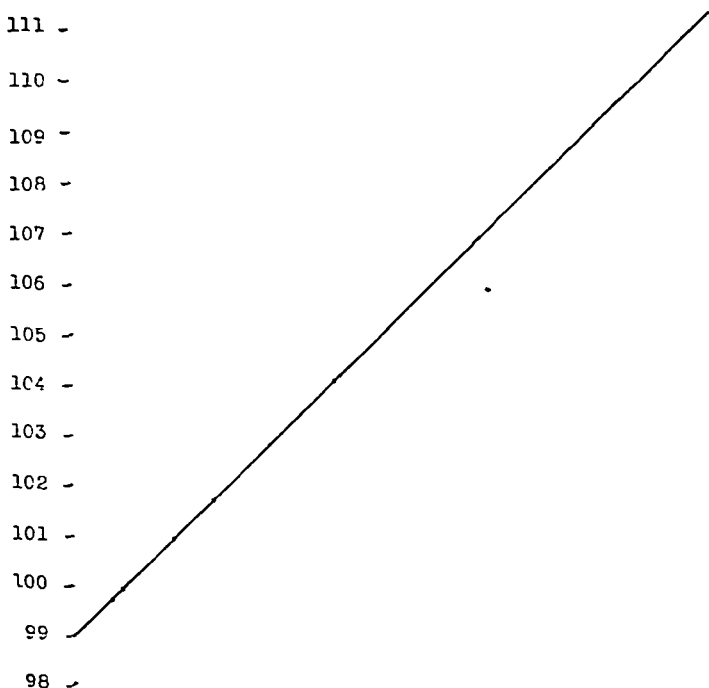


Chart 5—Distribution curve of temperatures of normal dogs compared with corresponding temperatures of dogs with tetanus with which they were paired for cross circulation. The temperatures of the normal dogs are plotted as dots in a vertical line crossing the corresponding temperatures of the dogs with tetanus, represented by the diagonal line.

of its causes. In other experiments (chart 3) significant differences in blood pressure were not associated with loss of blood from one animal to the other. In no instance during cross circulation did an animal with high blood pressure lose blood to one with a much lower pressure. These observations are rather surprising, since volume flow depends in part on the pressure gradient. That the cross section of the arteries anastomosed was likewise not the chief factor in the blood shift in the

few instances in which it occurred is suggested by the fact that there was considerable difference in the size of the carotid arteries in a number of experiments in which no loss of blood took place

SUMMARY

During cross circulation of dogs of approximately equal size no net loss of blood from one dog to the other was observed. In a few instances in which dogs with very different blood volumes were used for cross circulation a net loss of blood from the larger dog to the smaller took place. The arterial blood pressure is not the primary factor in the shift of blood. The loss of blood may be sustained by the animal with the lower pressure.

During cross circulation there is almost invariably an absolute increase in the combined total blood volume of the two animals, effected almost entirely by an increase in the total circulating red cell volume.

There is usually a definite fall in mean arterial blood pressure when the cross circulation is begun, after which there is a rise toward the normal level.

The pulse and respiratory rates of dogs during cross circulation may be different. The temperature of a normal dog rises when cross circulation is established between it and a dog with an experimentally induced fever (tetanus).

There is approximately complete mixing of the formed and chemical elements of the blood within two and one-half minutes after cross circulation is begun. If during cross circulation one chemical element (e. g., dextrose) is constantly supplied to the blood stream of one animal in greater quantity than to that of the other or if it is utilized by one dog more rapidly than by the other, the concentration will not be equal in the two animals.

INTRA-ABDOMINAL HERNIA

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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AND

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The literature on intra-abdominal hernia is composed for the most part of individual case reports, studies of limited groups of cases and reviews of special types of hernia. Moynihan and Dobson described various peritoneal fossae and made a fairly complete review of the cases of intra-abdominal hernia reported up to 1906. Short reviewed the cases reported between 1906 and 1915. In 1925 Short also reviewed cases in which there were clinical symptoms. No complete survey of the subject has been offered since 1906. Such a survey appears to us timely.

In this article we propose to review the entire subject of intra-abdominal hernia, report a unique case and make conclusions based on the experience with our own case and on the records of previously reported cases. We believe that such information, concretely assembled will be of value to others.

REPORT OF CASE

The patient was a 58 year old man, a cretin. He could not talk or write, and his mentality was about that of a 3 year old child. The persons who had him in their care noted that for the past few months he had suffered at irregular intervals from what were apparently intra-abdominal cramps, as he would grimace and hold his abdomen. His abdomen had for some years been somewhat protuberant, but lately the upper portion had become decidedly larger.

He was relatively active until three days before his admission to the hospital. At that time he complained that his belt was too tight, and he vomited an evening meal. After that he vomited 'coffee ground' material several times. He had a copious bowel movement the morning prior to the onset of acute symptoms, three days before admission, but none afterward.

Examination on admission revealed that the abdomen was distended and tympanitic throughout. There was a large, soft, balloon-like protrusion filling the space between the left costal margin and the umbilicus. Some peristalsis was heard in the lower part of the abdomen.

From the Laboratories of Pathology and Radiology, Columbia Hospital

The record of the case reported was made available by Drs. R. E. Morter and C. W. Long.

A grant from the Howard E. Mitchell Research Fund assisted in the preparation of this contribution.

The gastric contents were dark and sticky and gave a strong reaction for blood. The value for blood chlorides (as sodium chloride) was 511 mg per hundred cubic centimeters after administration of chloride. The urine was normal. The leukocytes numbered 11,000 per cubic millimeter.

Roentgen examination was made, with a presumptive diagnosis of an obstructing malignant lesion at the outlet of the stomach. A flat plate of the abdomen was first made. This revealed a large collection of gas in the left upper quadrant of the abdomen, sharply limited by a well defined wall. There was some dilated small bowel in the right upper quadrant. An attempt to insert a Wangensteen suction tube into the stomach under the fluoroscope failed.

The next day a small amount of barium sulfate was given. The stomach, instead of being dilated as expected, was found to be smaller than usual and displaced backward, upward and to the right. The gaseous mass had become larger. The barium sulfate ran slowly through the small bowel, which was dilated in some

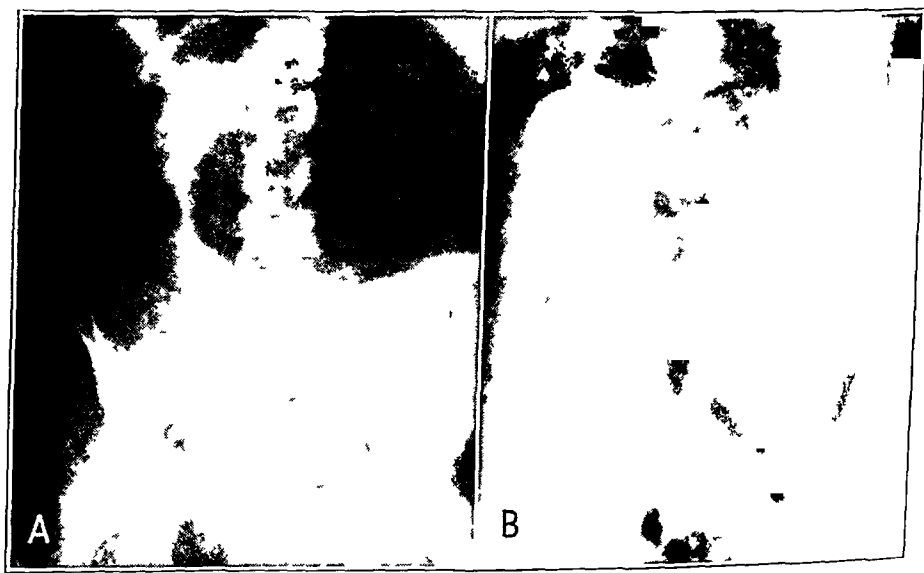


Fig 1—*A*, flat plate of the abdomen taken on admission of the patient to the hospital, showing a distended viscus in the left hypochondrium. This was thought at the time to be the stomach, distended with gas. *B*, roentgenogram taken a day later, after a small amount of barium sulfate had been administered. The gaseous accumulation was not in the stomach, but the stomach was displaced backward by it.

regions, and about twenty-four hours later was reported to have appeared in the stool. It was then deemed safe to give a larger amount by mouth. This was done, but no additional information was obtained until examination at the end of twenty-four hours, when thinly diluted barium sulfate was seen in the gas-filled sac. The sac was larger than before, and the barium sulfate suspension splashed around in it freely when the patient was turned or shaken.

A barium sulfate enema showed the colon to be in a relatively normal position except that its transverse portion was displaced upward and backward. The colon could not be examined well on the right side, but the hepatic flexure and the ascending colon seemed normal. The cecum was small but freely contractile. Owing to the difficulties of the examination, the small bowel was not well examined.

(This was unfortunate. The small bowel or the appendix should always be identified before a definite opinion is formed on an examination of the colon.) Dilated small bowel could be seen in the large sac, the size of which increased from day to day.

Roentgen examination was difficult and unsatisfactory because the patient was unable to help himself and because of his extremely low mentality. It was concluded that there was an obstruction in the lower part of the small bowel. The arrangement of the bowel suggested an internal retroperitoneal hernia, probably paraduodenal. The large, soft, balloon-like mass was thought to be due to distention of the lesser peritoneal sac, into which some part of the herniated bowel had perforated. It was recognized that the position of the stomach was opposed to this opinion, but the shape of the gas-filled mass suggested it.

The patient was under observation for several days, during which time he was not as ill as one would expect if an intestinal obstruction was present. A

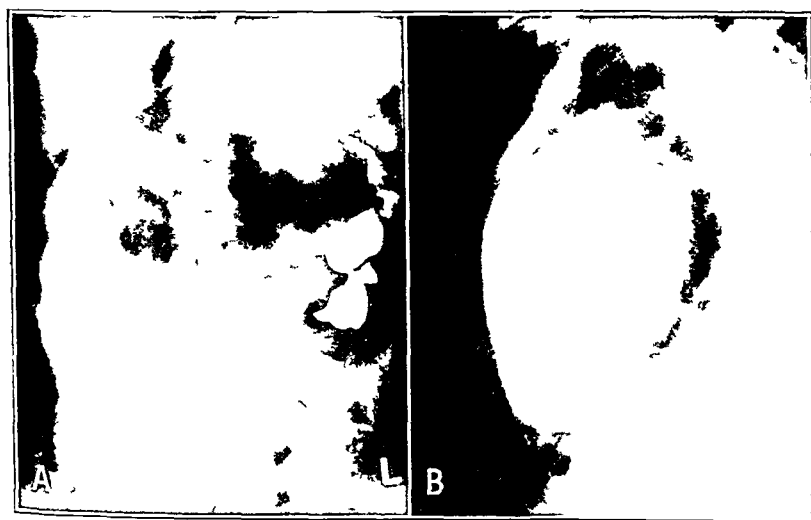


Fig 2—4, roentgen plate of the abdomen after twenty-four hours. The barium sulfate is distributed in dilated loops of small bowel. Note the barium water free in the large sac in the left hypochondrium. B, lateral view at this time, showing free barium solution in the large sac previously filled with gas.

preoperative diagnosis of intestinal obstruction, probably due to an internal hernia, was made.

At operation the abdomen was opened by an incision in the midline, and immediately a large, distended hollow viscus was seen. This was found to be the cecum, lying with its tip high under the left side of the diaphragm. It was enormously dilated and filled almost the entire upper portion of the abdominal cavity. It was fully 15 to 20 cm in diameter. Gas was aspirated from it until it was decompressed. Abdominal exploration was difficult on account of the size of the cecum and the distended loops of small bowel. However, a ragged opening was noted in the mesentery of the small bowel, through which emerged the dilated cecum.

The ascending colon was retracted inward, and at its external side was a hole through which two loops of bowel passed. These were pulled out. Several

feet of small bowel and, later, the dilated cecum were withdrawn. The condition of the patient was such that accurate or prolonged exploration was impossible. The assistant noted, however, that in the anterior edge of the inner hernial opening he felt the pulsation of a good-sized artery as he held the hole open during reduction.

The patient's postoperative condition was good until the fifth day, when signs of peritonitis were noted. He died the following day.

Postmortem examination revealed significant changes. The entire peritoneum which carried the viscera was relaxed and mobile. The great mesentery was long,



Fig 3—Roentgenogram taken after a barium sulfate enema. The examination was inconclusive and unsatisfactory. Note the colon draped over the gas-filled mass.

and the ascending colon and cecum were markedly mobile. The transverse mesocolon was long, but the descending colon was closely attached to the posterior abdominal wall. The foramen of Winslow was obliterated. The lesser peritoneal sac was normal except that the leaf of the transverse mesocolon, which constituted its floor, was elongated and scarred by linear striae. There were no important paraduodenal fossae. The stomach and duodenum were normal. The great mesentery was bifurcated by a deep digitation 18.9 cm from the duodenojejunal junction. The bowel above this point was normal, but distal to the

distention it had a thickened wall. This thickened portion of the small bowel was 138 cm long, and the loops were arranged together and were particularly adherent as if they had been contained in a sac.

There was a stoma 15 cm in length extending almost the entire length of the outer leaf of the mesentery of the ascending colon. The inner leaf of this mesentery where it reflected onto the upper leaf of the great mesentery had a linear rent 6 cm in length. This was definitely a tear, as there was no inversion of the serous lining which extended into the stoma previously mentioned. There was a sac extending into and distending the mesentery of the transverse colon as far as the greater curvature of the stomach.

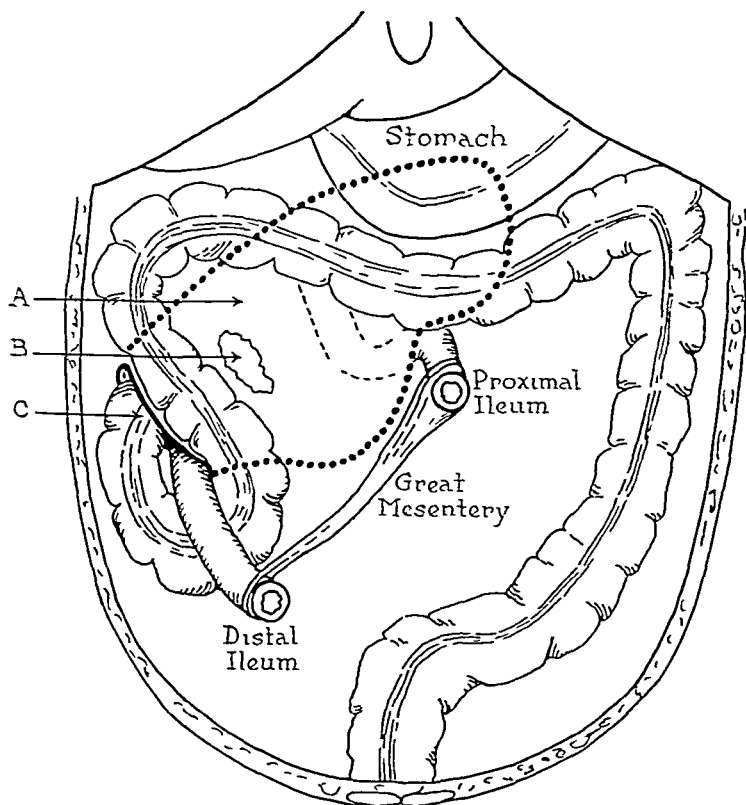


Fig 4—A, position and extent of hernial sac, B, rent in the inner leaf of the mesentery of the ascending colon, through which came the cecum, C, stoma in the outer leaf of the mesentery of the ascending colon, through which the hernia occurred.

Two small vesicles filled with slightly viscid clear fluid on either side of the trachea represented the thyroid.

INTERPRETATION OF CASE

The patient apparently had some type of internal hernia which was reduced at operation. An extended investigation was not expedient at

that time. When necropsy was performed the contents of the hernial sac had been withdrawn. An effort was made to reconstruct conditions as they existed prior to operation.

Certain facts were definite:

- 1 There was a large stoma in the external aspect of the mesentery of the ascending colon, with peritoneum reflected into the retroperitoneal space.
- 2 The cecum was very mobile because of an elongated mesentery.
- 3 Many of the peritoneal structures were remarkably relaxed, and the mesenteries were long.

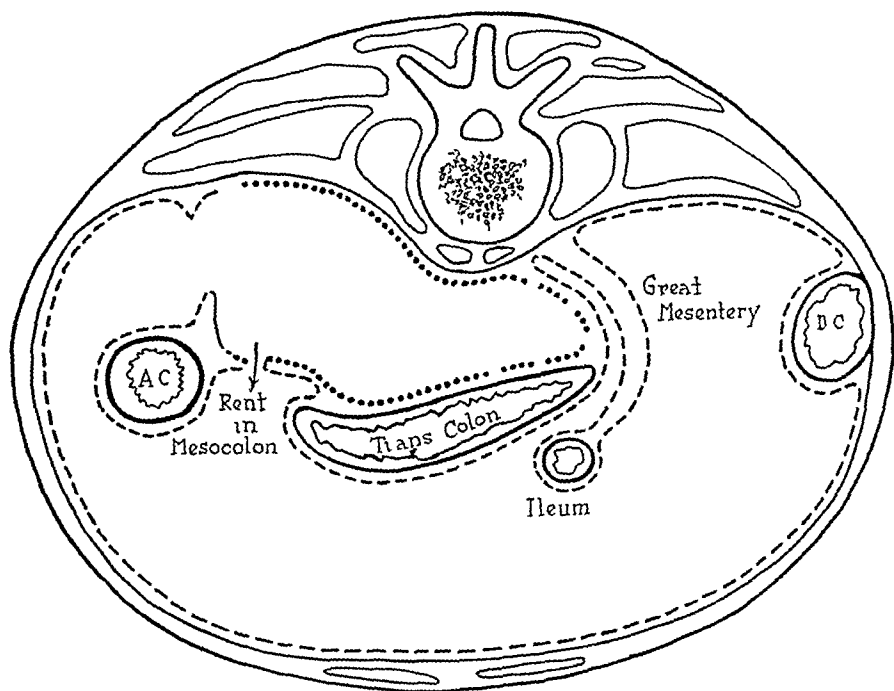


Fig 5—Diagram of a transverse section of the body at the level of the stoma, showing the position of the stoma, the rent in the mesentery and the extent of the hernial sac.

- 4 There was a rent in the inner leaf of the mesentery of the ascending colon at the point where this leaf was reflected onto the greater mesentery.
- 5 The great mesentery was bifurcated, and the lower 138 cm of the small bowel was adherent in a configuration suggesting confinement in a bag.

From these known facts and from the information gained by roentgen examination and by operation it seems logical to make the following interpretation of the conditions that existed prior to operation. There was a hernial sac extending into the retroperitoneal region, the opening

of which was in the lateral aspect of the mesentery of the ascending colon. This sac contained the cecum, the appendix and 138 cm. of small bowel, extending from the ileocecal valve to the distal ileum in the mesentery previously mentioned. The sac ruptured anteriorly through the peritoneum, where the ascending mesocolon was reflected on the great mesentery. The cecum had come out through the hole and had become enormously dilated so that it filled the whole left side of the abdomen.

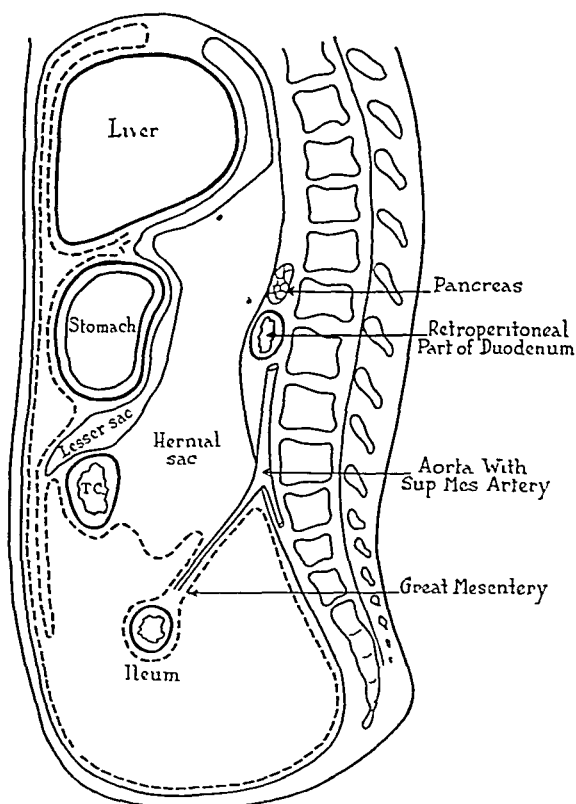


Fig 6—Sagittal diagram of the body, showing the position of the hernial sac.

It would seem that the patient had a congenital redundancy of the mesenteric structures. The hernia had probably been present for a considerable time, and perhaps the cecum broke through the wall at the onset of the present acute illness. The cecum became partially obstructed where it protruded through the rent in the mesentery, gas could get in but not out, which caused the cecum to become tremendously dilated.

The patient, then, had an internal hernia, rupture of the wall of which was followed by extrusion of the cecum from the hernial sac into the abdominal cavity with resultant partial intestinal obstruction.

Cullen reported a hernia in which the intestine entered the mesocolon of the ascending colon from its internal aspect. Short reported a case in which loops of the terminal part of the ileum entered a stoma from the lateral aspect at the junction of the cecum and the ascending colon. With the exception of a brief case report by Hacker, no description of a hernia entering the mesentery on the external aspect of the ascending colon proper has been found.

COMMENT

Classification of Hernias—Some of the reports in the literature contain incomplete descriptions of hernias, and the descriptions in others indicate that the hernias did not fit accurately into the described types. We endeavored from the information available to classify these hernias. The establishment of criteria was necessary. A hernia the stoma of which pointed upward and to the left and the sac of which dissected to the right beneath the superior mesenteric artery and entered chiefly the ascending mesocolon was considered a right paraduodenal hernia. A hernia the stoma of which pointed upward and to the right and the sac of which passed beneath the inferior mesenteric vein and left colic artery and came to occupy chiefly the descending mesocolon was considered a left paraduodenal hernia. A hernia the stoma of which pointed downward and the sac of which dissected the peritoneum of the left side of the abdomen from the posterior parietes was considered an infraoduodenal hernia. Needless to say, when the entire peritoneum was dissected from the posterior parietes we had only the configuration of the stoma for classification. The pericecal hernias included all hernias about the cecum, whether they were retrocecal, pericecal or subcecal (occurring as a pocket of peritoneum beneath the cecum). The ileocolic hernias were those which occurred in the angle between the ileum and the ascending colon. The ileoappendical hernias were those which occurred at the angle of the appendix, the cecum and the ileum. The prevesical hernias were those which occurred anterior to the bladder on either side of the remnant of the urachus and between the obliterated hypogastric arteries. The classification of other hernias should be self evident.

Most intra-abdominal hernias occur in or about the paraduodenal fossae, into the transverse mesocolon or through the foramen of Winslow.

Location and Incidence—Table 1 is a compilation of the locations of the reported hernias and indicates the sex of the patients so far as information on that was available.

These statistics are based on cases in which the diagnosis was proved. Cases in which there were unconfirmed roentgen diagnoses were not

included Cases in which hernia was associated with a previous surgical operation were not included Cases of which hernia pushed into other cavities or was destined to terminate outside the abdominal cavity were omitted The study was limited to instances in which hernia arose within the abdomen and appeared destined to remain within the abdomen

Miscellaneous cases were those in which the hernia occurred in one of the following ways behind an aberrant middle colic artery which arose from the common iliac artery, into the rectum, back of the pelvic peritoneum, into the properitoneal fat low on the anterior abdominal wall, into the mesentery of a mobile duodenum, back of the vitelline duct, through the mesentery of the falciform ligament of the liver, by a loop of small bowel pushing through a hole in an adjacent loop and (in 5 cases) by retroposition of the transverse colon the colon passing through the root of the mesentery

TABLE 1—*Incidence of Intra-Abdominal Hernia at Various Sites According to Sex as Recorded in the Literature*

Site	Cases	Males	Females	Sex Not Determined
Left paraduodenal	138	46	18	74
Transverse mesocolon	60	15	34	11
Right paraduodenal	47	28	6	13
Mesenteric	38	21	9	8
Foramen of Winslow	37	19	6	12
Pericecal	31	19	4	8
Intersigmoid	28	20	7	1
Broad ligament	18		15	
Ileoappendicular	16	13	3	
Ileocolic	14	8	6	
Prevesical	13	3		10
Inferior duodenal	5	2	2	1
Great omentum	5	3	1	1
Ascending mesocolon	4	4		0
Miscellaneous	13			
Totals	467	200	116	151

More of the intra-abdominal hernias occurred in men than in women but hernia of the transverse mesocolon was found oftener in women An intra-abdominal hernia occurring in the pelvis of a woman is almost certain to be into the broad ligament

The regional distribution of the reported hernias is summarized in table 2 There it is indicated that hernia is most frequently found about the duodenum underneath the transmesocolon The foramen of Winslow is frequently mentioned as a common site for intra-abdominal hernia but from the table it will be seen that this site was not concerned in a high percentage of cases It is further stated that hernia into the foramen of Winslow is associated with an abnormally mobile cecum In this study that statement was found erroneous

A roentgen diagnosis of a sizable intra-abdominal hernia may be made with some degree of accuracy but it would seem that the roentgen

determination of the site of the stoma is not much more accurate than a statistical guess. The roentgen features of right paraduodenal hernias were well described by Eaker. From the reports of the various types of hernia which were diagnosed by roentgenograms, certain roentgen signs seem to have been present. There was a disturbance of the normal intestinal arrangement. In some cases the displaced intestines remained crowded together as if contained in a bag. There were dilatation and loss of mobility of the affected loops of bowel associated with a varying degree of stasis.

Mechanism—Intra-abdominal hernia may occur at almost any age and at almost any place in the abdomen. The only supports for the peritoneal reflections are the parietes, the vessels and the nerves. Most articles elaborate on the location of various fossae, but it must be pointed out that hernia may take place at any point where the peritoneum is not defended by the parietes or by the vessels and nerves in the mesentery. It would appear that both fossa and hernia are expressions

TABLE 2—*Regional Distribution of Reported Hernias*

Region	Number	Percentage
Paraduodenal	250	53
Pericecal and terminal ileum	61	13
Perimesenteric	38	8
Foramen of Winslow	37	8
In the pelvis	31	7
In the sigmoid region	28	6
Miscellaneous	22	5
Total	467	100

of regional peritoneal weakness rather than that the fossa acts in a causative way in the development of a given hernia. At least, the stomas of the reported hernias did not always conform precisely to the described peritoneal fossae.

In the case reported in this paper the hernia broke through the hernial sac back into the abdominal cavity. With the more common hernias in and around the paraduodenal fossae this rarely occurs, but it not infrequently occurs with the other varieties, particularly those entering the mesenteries or the foramen of Winslow.

The controversy as to whether hernias are congenital or acquired cannot be decided in individual cases. Certain facts, however, may be stated. Some hernias, particularly left paraduodenal, are found in newborn infants. Some hernias are dependent on abnormal mesenteries, mesenteric holes and aberrant vessels. Retroposition of the transverse colon could occur only during development of the peritoneal reflections. However, intra-abdominal hernias occur after surgical procedures, particularly those involving the transverse mesocolon. It seems certain that both mechanisms are responsible for intra-abdominal hernias.

Treatment and Prognosis—Surgical treatment of intra-abdominal hernia is usually indicated, and recently the results here compare favorably with those obtained with other hernias

Reduction of the hernia is about all that is necessary. Elaborate efforts to close the opening unless there is a large hole directly through a mesentery, are usually not necessary as stomas are usually roughened, and agglutination of adjacent folds of peritoneum occurs quickly. In only 1 case was a recurrence noticed, it occurred through a large

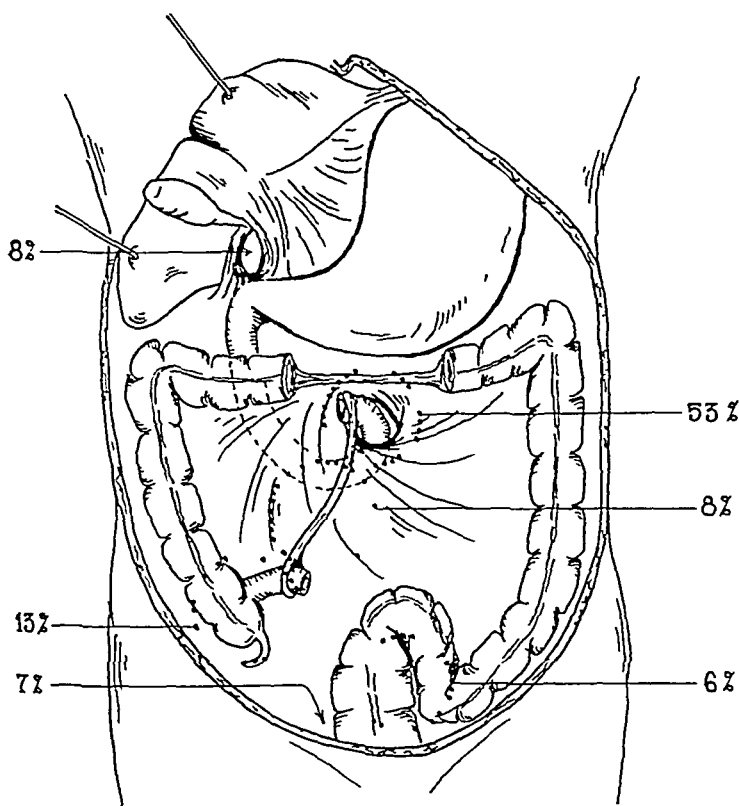


Fig 7—Diagram of the abdomen showing the frequency (expressed in percentage) of intra-abdominal hernias in various regions of the abdomen

foramen of Winslow, but it caused no symptoms and was observed incidentally at postmortem examination

The general condition of the patient, the condition of the circulation of the involved intestine and the amount of injury to the intestinal wall are the important points in surgical prognosis

The tables indicate to the surgeon and the pathologist that in most instances the stoma of intra-abdominal hernia will be found by lifting up the transverse mesocolon and exploring the paraduodenal region

They show also that hernia in the broad ligament and hernia through the transverse mesocolon are important in women and that hernia in the pelvis is almost always in the broad ligament. The information contained in the tables should assure an intelligent exploration of the abdomen of a patient of either sex at operation or at postmortem examination.

In attempting to determine the exact site of the stoma, its relation to the left colic artery and the inferior mesenteric vein or to the superior mesenteric artery is important. Finally in exploration of the abdomen for internal hernia one should always consider abnormal intestinal rotations and aberrant vessels.

BIBLIOGRAPHY

A classified bibliography has been prepared. This includes general reviews of the whole subject and special reviews of hernia occurring in special locations. Some important roentgen studies are included. By reference to the bibliography, excellent articles on all forms of intra-abdominal hernia can be obtained.

SUMMARY

An unusual case of retroperitoneal hernia occurring in the external leaf of the mesentery of the ascending colon is reported.

The literature is reviewed, and tables are presented to show the location and frequency of all forms of intra-abdominal hernia.

The roentgen diagnosis of the condition is fairly accurate, but the roentgen determination of the site of the stoma is not reliable.

The treatment is surgical, and good results follow simple reduction of the hernia.

A classified bibliography is presented.

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HEMANGIOMA OF THE COLON

REPORT OF A CASE

C F SAWYER, MD

CHICAGO

Tumors of the blood vessels are numerically important among the neoplasms found in the human body. Many of these are benign angiomas of the body surfaces and merit little special clinical attention.

Hemangiomas of the capillary, or simple, type are characterized by an intricate arrangement of capillary blood vessels embedded in a variable amount of connective tissue stroma. They are usually congenital and may involve any part of the body except the cornea and cartilages. Although benign, they may be associated with malignant disease. They may be circumscribed or diffuse.

Cavernous hemangiomas are composed of blood spaces of irregular shapes and sizes which communicate with each other and are supported by a connective tissue framework. The spaces are lined with endothelium. The tumors are sometimes pulsating and erectile.

Many pathologists do not consider hemangiomas of either type as true tumors, classifying them instead as malformations. This is because many hemangiomas are supposed to lack the power of independent proliferation. This is not true of a third type, however, which may show either the capillary or the cavernous arrangement or both in the same tumor. The hypertrophy is mostly evident in proliferation of the endothelial cells. Although not always encapsulated, most of these neoplasms are benign. Some of them become definitely malignant and are classified as endothelial sarcomas. Even though benign, they may cause local destruction through their manner of extension (by infiltration of the adjacent tissues) and by their growth along the blood vessels.

Geschickter and Keasbey¹ classified 570 hemangiomas as regards distribution in the body. Three hundred and seventy of these were peripherally located. Sixty-five were grouped under "special locations" including the bones, the muscles and the central nervous system. The remaining 135 were included in a "central group," 109 occurring in the liver, 16 in the heart valves and only 10 in peritoneal or retroperitoneal structures, namely, the mesentery, the kidney, the spleen and the gastrointestinal tract. If these statistics represent a fair cross section of the

¹ Geschickter, C. F. and Keasbey, L. E. Tumors of Blood Vessels. *Am J Cancer* 33: 568-591 (March) 1935.

distribution of hemangiomas, it is apparent that the tumors are rarely found in the intestines

In 1930, McClure and Ellis² collected 24 cases of hemangioma of the intestines from the literature and reported 1 of their own. In 14 of these cases the tumor was single, and in 11 there were multiple hemangiomas. The tumors were distributed as follows: 2 in the duodenum, 15 in the small intestine below the duodenum, 1 in the colon, 4 in the rectum and 2 in the entire bowel. The location of 1 was not stated.

Bargen and Dixon³ said "This is perhaps the rarest type of tumor in the large bowel." They mentioned the occurrence of hemangiomas as follows: 1 in the wall of the cecum, discovered in an operation for

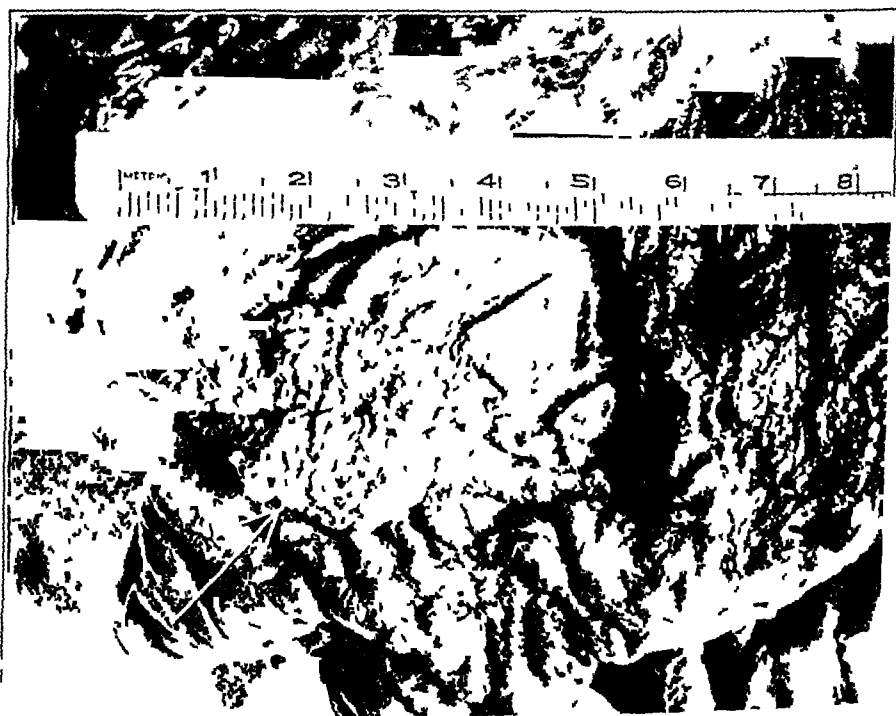


Fig 1—Photograph of the gross specimen. The arrow indicates the location of the tumor. 12

gallstones, 1 in the splenic flexure, with a preoperative diagnosis of carcinoma, and 2 in the rectosigmoid region, with a preoperative diagnosis of polyp.

These tumors usually arise in the submucosa. They may grow toward the lumen of the intestine, become ulcerated and cause hemorrhage. They may grow to such a size in the lumen as to cause mechanical obstruction. They may infiltrate the muscle wall and by ringlike contraction and constriction of the lumen cause an intestinal obstruction.

2 McClure, R. D., and Ellis, S. W. Hemangiomas of Intestines, *Am J Surg* 10: 241-244 (Nov.) 1930.

3 Bargen, J. A., and Dixon, C. F. Uncommon Tumors of the Large Intestine, *Am J Digest Dis & Nutrition* 1: 400-403 (Aug.) 1934.

Such growths may be symptomless, and no doubt some are not discovered. A sign of hemorrhage is the most frequent finding. This may be only a slight staining with blood or a massive hemorrhage. Signs of intestinal obstruction, either acute or chronic, may or may not be associated with the hemorrhage. Infrequently hemangiomas may be found elsewhere for example in the skin, and may suggest similar lesions in the bowel. Roentgen examination is likely to confirm obstructive signs.

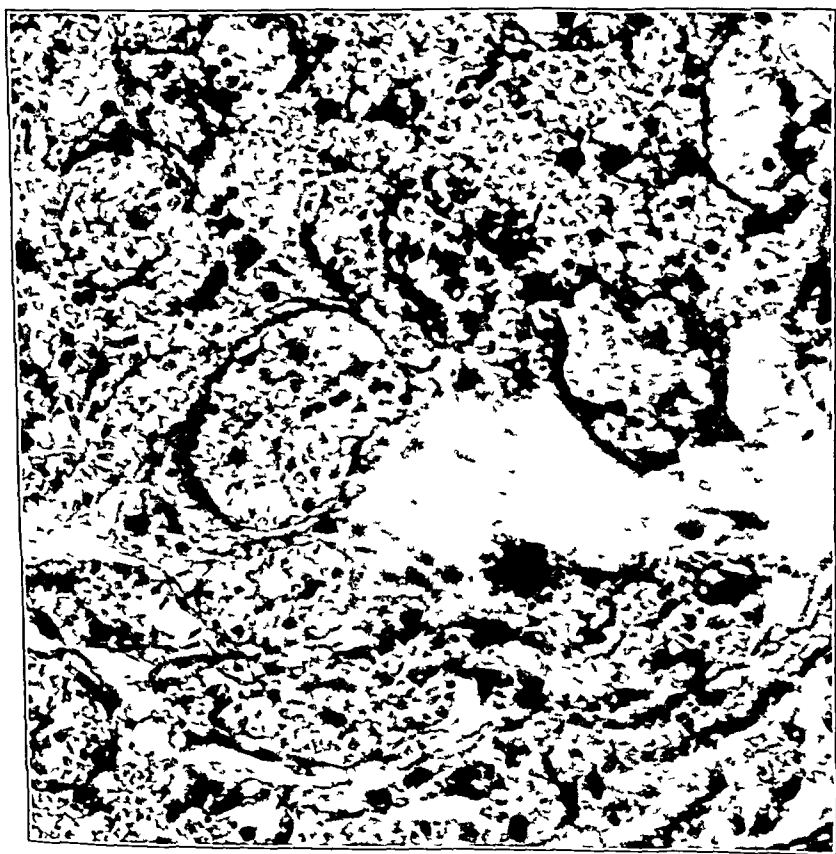


Fig 2—Microscopic section through the tumor, showing well defined capillaries filled with red cells. Note the masses of red cells between the capillaries (hemorrhage).

but is not of much value in differentiation of the condition from carcinoma.

In the presence of obstruction surgical treatment is indicated. The mortality is high as was indicated by Brown⁴ in his review of 20 cases.

⁴ Brown A. J. Vascular Tumors of the Intestine. Surg. Gynec. & Obst. 39:101-100 (Aug.) 1924.

of hemangioma of the intestinal tract below the stomach. Of this number, death occurred in 14 and recovery in 5. In 1 the result was not stated. This report covered a period of seventy-five years. Modern surgery should make a better showing.

REPORT OF CASE

I G, an unmarried steel worker aged 55, entered Mercy Hospital March 21, 1935, in the service of Dr F M Drennan. His complaints at the time of admission were severe intermittent pain in the lower part of the abdomen, no effective bowel movement in seven days, some blood noted in the stools previously, and loss of 10 pounds (4.5 Kg) in weight. For three and one-half months he had had attacks of cramplike pain in the lower part of the abdomen, associated with stubborn constipation. The attacks at first occurred at intervals of about one week, and relief was obtained with enemas. Gradually the attacks became more severe and occurred at shorter intervals. When an enema was given the pain was at first increased, and then, with the flushing out, it largely disappeared. At first the relief lasted for several days, but later it lasted only for a few hours and the patient could not take as much water as formerly. He had never had a black stool, but recently he had noted a little red blood. Loss of 10 pounds (4.5 Kg) in weight had occurred in the last year, but his appetite had been fair until the last few days. He stated that ever since the Spanish-American War he had been bothered by constipation and had taken a laxative nearly every day. He rarely had a headache. His eyes were good. He was somewhat deaf. He had no trouble with his nose, throat or chest except for an occasional cough. There was no epigastric distress. There were no symptoms referable to the genito-urinary tract. About two years previously he had had pain in both elbows. This was relieved when his teeth were removed. For twenty years after a strain incurred while wrestling he had had occasional pain in the region of the right hip, but this was less troublesome than before the extraction of his teeth.

Examination of the head, neck and chest gave essentially negative results. The abdomen, though not distended, was tense, and there was apparent tenderness on the left side. There was a suggestion of a mass to the left of the umbilicus. The liver, spleen and kidneys were not palpable. Digital rectal examination gave negative results. The blood count showed 5,370,000 red cells and 9,450 white cells per cubic millimeter, with 70 per cent hemoglobin. The Wassermann reaction of the blood was negative. Urinalysis gave essentially negative results. Of seven stools obtained by enemas, examination showed no blood in three, in the other four a variable amount was present (up to 4 plus). Roentgen examination after a barium sulfate enema caused considerable distress. The rectal ampulla was larger than normal. In the upper part of the sigmoid flexure and the lower part of the descending colon a definite obstruction was noted, which allowed only a thin stream of barium to pass through. At the point of obstruction there was apparently a definite, palpable mass which was tender to pressure. A roentgenogram taken immediately afterward revealed a definite filling defect in this area.

The patient was referred by Dr Drennan for operation on April 1. An incision was made near the outer border of the left rectus muscle. A constricting neoplastic mass was found in the lower part of the descending colon. It was not fixed posteriorly or adherent to other structures. There were many hard, shotlike glands in the mesentery. No pathologic change was noted in the liver or other abdominal organs. By means of a Mikulicz exteriorization procedure the involved loop of

bowel was free and delivered outside the abdominal wall. The entire mass was removed by cautery the following day. The patient's convalescence was uneventful, and he left the hospital May 8 with an almost normally functioning bowel. A small fistulous opening was successfully repaired some months later.

Pathologic Report—The section of the large bowel examined was 21 cm long. Nine centimeters of this section of bowel was a healthy pink, and this normal area was sharply demarcated from the remaining 12 cm of densely edematous and dark red hemorrhagic portion. Six centimeters from the end of the latter portion there was a friable tumor mass 2.5 cm in diameter, elevated to a height of 5 to 7 mm. It had a broad base and was sharply demarcated. The surface was friable and somewhat papillomatous. It was of the same dark red color as the intestine. Microscopic examination of the tumor revealed a capillary hemangioma of the mucosa. The tumor with the rest of the dark red portion of the intestine had undergone hemorrhagic infarction. The masses along the mesentery were chronically inflamed lymph nodes and some had undergone hemorrhagic degeneration. The diagnosis was capillary hemangioma of the bowel with hemorrhagic infarction.

COMMENT

The tumor in this case simulated an obstructing carcinoma of the large bowel in almost every particular. The entire absence of blood in several stools and its presence in fairly large amounts in two others would seem the only discrepancy. The hemorrhage has been the prominent finding in the few cases of hemangioma of the large bowel previously reported. This case, more than any other, emphasizes the obstructive symptoms.

EFFECTS OF ESTROGEN ON BONES, JOINTS AND LIGAMENTS OF CASTRATED GUINEA PIGS

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AND

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It has been shown that estrogens cause definite gross anatomic alterations in the joints of the pelvic ring in the guinea pig¹ Hisaw² has demonstrated experimental relaxation of the pubic symphysis with the relaxative hormone of the corpus luteum Little attention, however, has been paid to the minute histologic changes occurring at the pubic symphysis during the transformation Furthermore, similar correlative histologic studies of other bones and joints of guinea pigs are lacking³

In the light of these facts it seemed of interest to investigate the effects of subcutaneous injections of estrogen⁴ in mature castrated guinea pigs on (1) the tissues of the pubic symphysis and the sacroiliac

From the Laboratory Division of the Hospital for Joint Diseases

1 de Fremery, P, Kober, S, and Tausk, M Erweiterung der Symphysis pubis des weiblichen Meerschweinchens durch Menformon, Acta brev Neerland **1** 146, 1931 Tapfer, S, and Haslhofer, L Hormonale Weiterstellung des Beckens im Tierversuch, Arch f Gynak **159** 313, 1935 Gardner, W U Sexual Dimorphism of the Pelvis of the Mouse The Effect of Estrogenic Hormones upon the Pelvis and upon the Development of the Scrotal Hernias, Am J Anat **59** 459, 1936

2 Hisaw, F L The Influence of the Ovary on the Resorption of the Pubic Bones of the Pocket Gopher, Geomys Bursarius (Shaw), J Exper Zool **42** 411, 1925, Experimental Relaxation of the Pubic Ligament of the Guinea Pig, Proc Soc Exper Biol & Med **23** 661, 1926, Experimental Relaxation of the Symphysis Pubis of the Guinea Pig, Anat Rec **37** 126, 1927, The Corpus Luteum Hormone Experimental Relaxation of the Pelvic Ligaments of the Guinea Pig, Physiol Zool **2** 59, 1929 Fevold, H L, Hisaw, F L, and Meyer, R K The Relaxative Hormone of the Corpus Luteum, J Am Chem Soc **52** 3340, 1930, Isolation of the Relaxative Hormone of the Corpus Luteum, Proc Soc Exper Biol & Med **27** 604, 1930, Physiology of the Corpus Luteum, in Allen, E Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1932, p 499

3 Tausk, M, and de Fremery, P Ueber den Einfluss des Follikel Hormons (Menformon) auf die Ossifikation bei kastrierten Hunden, Acta brev Neerland **5** 19, 1935 Zondek, B Impairment of Anterior Pituitary Functions by Follicular Hormone, Folia clin orient **1** 1, 1937 Gardner, W U, and Pfeiffer C A Skeletal Changes in Mice Receiving Estrogens, Proc Soc Exper Biol & Med **37** 678, 1938, Inhibition of Estrogenic Effects on the Skeleton by Testosterone Injections, ibid **38** 599, 1938

4 Estradiol benzoate in sesame oil was supplied by the Schering Corporation

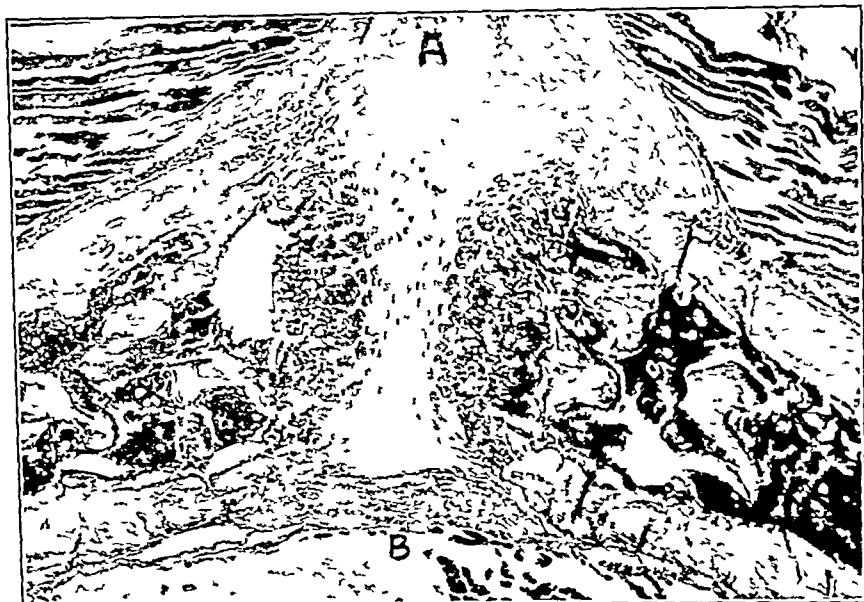


Fig 1—Photomicrograph of a normal pubic symphysis A, anterior ligament, B, posterior ligament.



Fig 2—Photomicrograph of a sacroiliac joint Note the interdigitating ligamentous bands (arrow) $\times 20$

joints in situ, (2) autogenous transplanted segments of the pubic symphysis with attached ligaments, and (3) the capsular tissues of the major joints

METHOD

Twelve male guinea pigs, each weighing approximately 400 Gm, were castrated under general anesthesia. In 8 animals the lower caudal half of the pubic arch, consisting of parts of the right and left pubic rami with the attached muscles and ligaments, were removed and transplanted into an artificial pocket made in the abdominal wall. In the remaining 4 the entire pubic arch was left in situ. Four additional guinea pigs served as controls, undergoing neither castration nor transplantation and receiving no injections of estrogen. The 12 castrated guinea pigs were divided into three groups of 4 animals each. The experimental conditions in the three experimental groups are given in the accompanying table.

At the end of the experiments the animals were killed with ether and roentgenographed. The original and transplanted portions of the pubic symphysis were

Experiments with the Injection of Estrogen in Guinea Pigs

Group 1 (testes removed, no transplantation, injection of estrogen)	
Duration of Experiment, Days	Total Estrogen, Rat Units
28	12,000
31	23,000
60	51,000
80	60,000
Group 2 (testes removed, transplantation, no injection of estrogen)	
Duration of Experiment, Days	Total Estrogen
28	None
31	None
60	None
80	None
Group 3 (testes removed, transplantation, injection of estrogen)	
Duration of Experiment, Days	Total Estrogen, Rat Units
28	12,000
31	23,000
60	49,000
80	60,000

removed, roentgenographed, fixed in Helly's fluid⁵ and sectioned. Sections were taken also from the skull (including the symphysis menti and the incisors), sacroiliac articulations, hip, knee and vertebral column.⁶ All sections were embedded

5 Helly's fluid consists of potassium bichromate, 2.5 Gm, mercury bichloride, 5 Gm, and water, 100 cc. To 90 cc of this solution 10 cc of a 40 per cent solution of neutral solution of formaldehyde U S P is added just prior to the fixation of the tissues.

6 To realize the effects of the injections of estrogen, it is necessary to be familiar with certain fine points in the anatomy of the pubic symphysis and sacroiliac joints of the male guinea pig. The pubic bones are separated by a sheet of hyaline cartilage. The cartilage rarely shows cracks or fissures, especially if the animal is young. The pubic bones are held together by the thick anterior ligament and the thin posterior ligament (fig 1). Elastic fibers extend from the periosteum of one bone through the anterior and posterior ligaments respectively to the opposite bone. The sacroiliac joints consist of two parts, the anterior, or true, joint and a posterior segment consisting of interdigitating cross bands of ligaments. These bands insert into the elastic layer of the periosteum of the sacrum and ilium. Numerous thin-walled blood vessels are observed between these fibrous bands (fig 2).

in paraffin and stained with hematoxylin and eosin. In addition, some of the preparations were stained for elastic fibers.

RESULTS

GROUP 1 (castration, no transplantation, injections of estrogen)—In this group the subcutaneous injections of estrogen induced no grossly obvious change in the



Fig 3—Photomicrograph of the symphysis menti. The structure shows no alterations following the subcutaneous injection of 51,000 rat units of estrogen over a sixty day period $\times 30$.

capsules of the hip or knee joints. The results were negative also in the symphysis menti (fig 3), the frontal bones, the joints of the vertebral column, the sacroiliac articulations and the incisors. The epiphyseal cartilage plates of the long bones appeared to have been closing somewhat prematurely. The roentgenograms revealed no striking alterations in the density of the skeleton.

In the symphysis pubis, however, definite alterations were encountered in one guinea pig after as little as 23,000 rat units had been given over a period of



Fig 4—*A*, photomicrograph of a section through the untransplanted pubic symphysis, showing thickening and hypercellularity of the posterior ligament (*P*) Note the cracks in the interpubic cartilage The animal received 23,000 rat units of estrogen over a period of thirty-one days $\times 35$ *B*, photomicrograph of another section of the same pubic symphysis, disclosing marked thickening and hypercellularity of the posterior ligament (*P*) Note the resorption of the posterior cortices $\times 35$

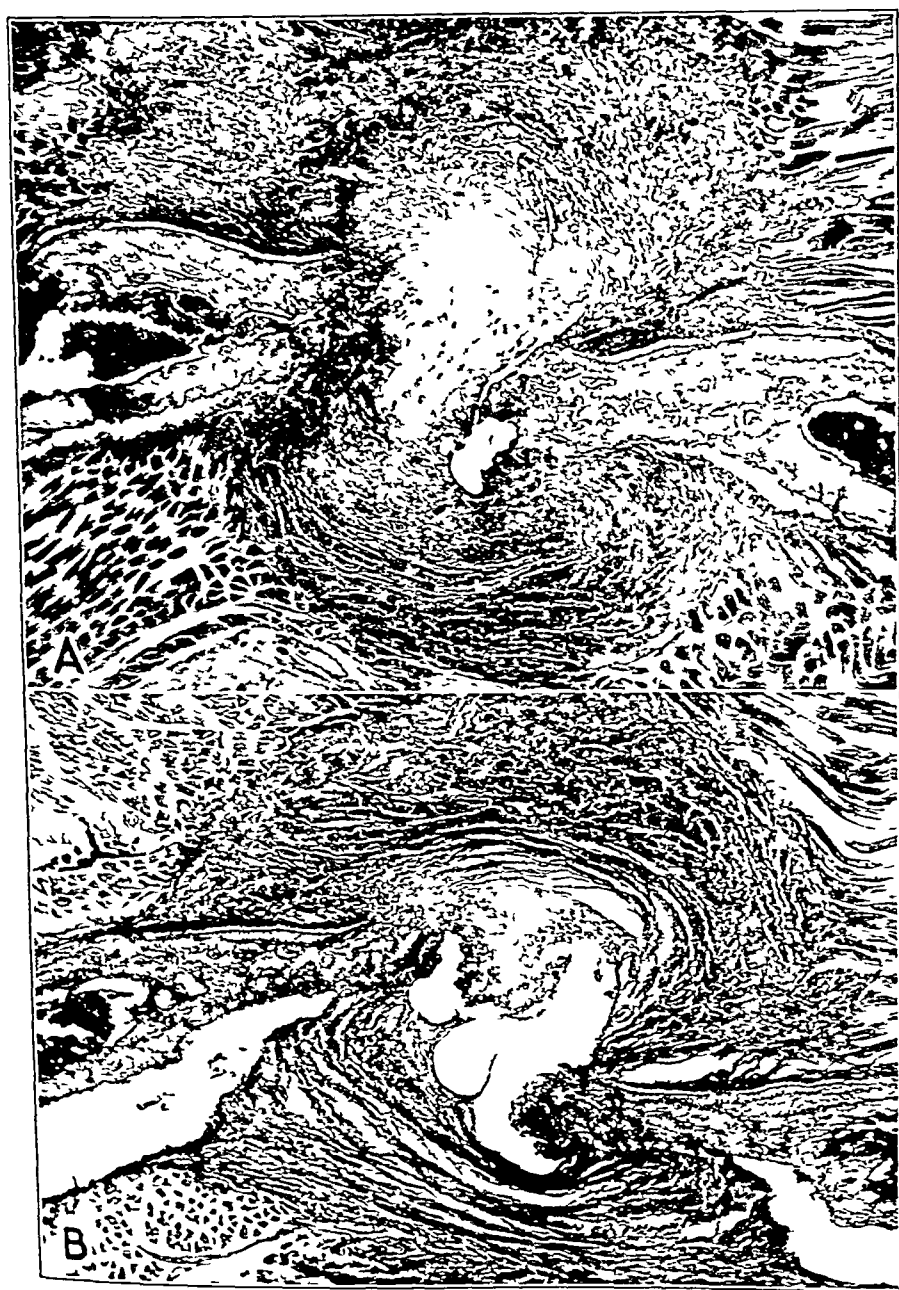


Fig 5—*A* photomicrograph of a section of the untransplanted pubic symphysis showing thickening and hypercellularity of both the anterior and the posterior ligaments. Note the lytic changes in the interpubic cartilage. The animal received 51,000 rat units over a period of sixty days. $\times 35$ *B* photomicrograph of another section of the same pubic symphysis, showing advanced lytic changes of the interpubic cartilage with a posterior displacement of the right pubic bone. $\times 35$

thirty-one days. The posterior ligament became thickened and hypercellular and rapidly replaced the interpubic cartilage. The latter underwent degeneration resulting in fissures and small cysts. The pubic bone bore evidence of resorption even on its posterior cortex (fig 4). In another animal, which received 51,000 rat units of estrogen over a period of sixty days, the advanced lytic changes in the pubic symphysis had caused a definite separation of the pubic bones, with a posterior displacement of one of them (fig 5). In an animal which received 60,000 rat units of estrogen additional changes were observed. The anterior cortices of the pubic bones showed resorption, and the elastic fibers in the posterior pubic ligament were fibrillated, cracked and widely scattered.

GROUP 2 (castration, transplantation of part of the pubic arch, no injection of estrogen).—In the 4 animals of this group no significant changes were observed



Fig 6—Photomicrograph of the transplanted portion of a pubic arch, showing partial necrosis of the interpubic cartilage. The anterior and posterior ligaments present no striking alterations. The animal received no injections of estrogen. The transplant was eighty days old. $\times 30$

in the ligaments or bones of the original, untransplanted segment of the pubic arch. The posterior ligaments showed some reparative thickening. In the animal killed at about twenty-eight days the transplanted piece was largely necrotic. The growth plates in the transplanted segments of the pubic bones were inactive. No demonstrable alterations were observed in the posterior ligaments. In the animal killed thirty-one days after transplantation some of the nuclei of the transplanted pubic cartilage appeared to be alive, and there was considerable evidence of transformation and rebuilding of the dead cortical bone. The intertrabecular marrow spaces had been undergoing fibrosis. In one of the preparations the posterior ligament was slightly cellular. Another transplant, examined eighty days after implantation,

tion, showed almost complete acellularity of the ligaments. Most of the interpubic cartilage was necrotic (fig 6)

GROUP 3 (castration transplantation of part of the pubic arch injections of estrogen)—The transplanted segment of the pubic arch displayed nothing unusual after thirty-one days, even when the animal had received 23,000 rat units of estrogen. The original, untransplanted portion of the arch showed thickening of the posterior ligament and active resorption of the posterior portion of the interpubic cartilage. Another transplant, examined sixty days after implantation in the case of an animal which had received 49,000 rat units of estrogen, revealed

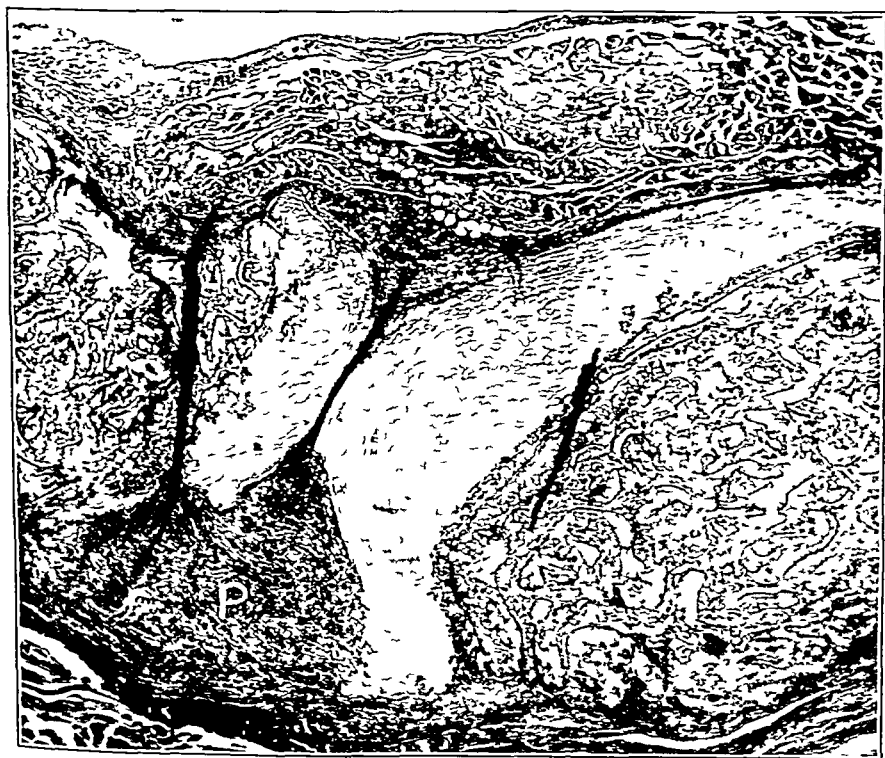


Fig 7—Photomicrograph, $\times 15$, of the transplanted portion of the pubic arch. Note the thickening and hypercellularity of the posterior ligament (*P*). Note also the necrosis and resorption of the interpubic cartilage. The pubic bones are undergoing transformation. The animal received 60,000 rat units of estrogen over a period of eighty days. The transplant was eighty days old.

distinct thickening and cellularity of the posterior ligament. It showed that active resorption of the interpubic cartilage had been proceeding at a rapid rate. The original untransplanted segment of the pubic arch revealed active proliferation of the posterior ligament and re-absorption of the posterior cortices. In another animal, which had received 60,000 rat units of estrogen, examination of the transplanted pubic arch eighty days after the implantation revealed definite hypercellularity of the ligaments and resorption of the posterior cortices (fig 7). Much more active transformation had occurred however in the untransplanted segment

Here the interpubic cartilage was undergoing cystic degeneration in some places and, in addition, was being resorbed by the highly cellular ligaments

SUMMARY AND CONCLUSIONS

This study represents an experimental investigation of the effects of estrogen on castrated male animals, particularly on their skeletons. The subjects were male guinea pigs weighing about 400 Gm each. Of the 12 animals, 8 were given injections of estrogen, and in 4 of these 8 transplantation of part of the pubic symphysis was performed. Four additional guinea pigs served as controls. The duration of the experiments was twenty-eight to eighty days, and the total amount of estrogen administered was 12,000 to 60,000 iat units.

The experiments show, first, that castrated male guinea pigs can be successfully feminized by injections of estrogen, the feminization being revealed in enlargement of the nipples and the formation of areolas. As to the skeleton, no striking alterations were observed in the capsules of the major joints, in the epiphysial plates, in the costochondral junctions, in the symphysis menti or in the sacroiliac articulations. It was in the region of the symphysis pubis that the estrogen exerted its striking effect. The ligaments, especially the posterior ones, became hypercellular, increased in thickness and invaded the interpubic cartilages and the posterior cortices of the pubic bones. In some instances the interpubic cartilages underwent secondary degenerative changes resulting in the appearance of slits. Even in transplanted segments of the pubic arch the posterior ligaments became hypercellular when the animals received sufficient quantities of estrogen. In the animals which did not receive estrogen the posterior ligaments of transplants of pubic bone underwent little or no change. Apparently the pubic ligaments, especially the posterior one, are affected in a specific way by estrogen. The interpubic cartilage partakes in the changes, but its reaction seems to be influenced to a great extent by that of the pubic ligaments. The lack of reaction in the ligaments of the sacroiliac joint is striking.

RESPIRATORY PHYSIOLOGIC PHENOMENA DURING INHALATION ANESTHESIA

EDWARD B TUOHY, MD

ROCHESTER MINN

This paper concerns some of the important features of anesthesia induced by various gases from the standpoint of preoperative medication physiologic phenomena associated with administration of most inhalation anesthetic agents and supportive measures for the patient during anesthesia

In order to allay fear and promote rest it is customary to administer a sedative agent to most patients before the operation. Usually morphine sulfate is administered, because it promotes rest and diminishes the patient's perception of pain. Although as a rule opium derivatives do not produce sleep unless given in large doses they do enhance the effect of most soporific drugs, such as bromides and barbiturates. For this reason it is common practice to use such agents as pentobarbital sodium, sodium amytal and various other barbiturates and bromide preparations in conjunction with opiates. The different drugs of the atropine series, such as belladonna, atropine sulfate and scopolamine are used routinely to inhibit secretion of mucus during inhalation anesthesia, to inhibit parasympathetic (vagus nerve) activity and to antagonize the metabolic depressant action of morphine.

The dose of any drug, especially when used for premedication purposes, should be sufficient to produce a safe pharmacologic effect. I do not believe that it is possible to state a specific dose for every patient. As the basal metabolic rates of patients vary widely, it is important to bear in mind that the different drugs vary diversely in the intensity of their action. In other words, whereas for one person a given dose of morphine sulfate or of a barbiturate is insufficient to produce a pharmacologic effect, for another person the same quantity of the same agent constitutes an overdose. It is suggested therefore, that a more accurate method for administering premedication agents be employed. To certain patients one should administer small doses of the drug preoperatively and repeat them whenever necessary to produce the desired effect. Furthermore, one should not begin administration of an inhalation anesthetic in most instances until a reasonable time has been allowed for the agents given orally and hypodermically to produce their optimal effect.

From the Section on Anesthesia the Mayo Clinic

The mechanism of inhalation anesthesia is complex and depends on many factors. Some of the most important of these are the physical laws which determine diffusion of gas and vapors and the anatomic, physiologic and chemical considerations incident to respiration. During induction of anesthesia with an inhalation anesthetic the concentration, or partial pressure, of any given anesthetic agent is higher in the alveolar air than is the partial pressure of the agent in the blood and tissue. The rate of diffusion of the anesthetic into the blood stream is rapid at first, depending, of course, somewhat on the area of alveolar membrane exposed to the gas and the rapidity of pulmonary circulation. As the concentration of the anesthetic rises in the blood, the rate of its diffusion from the alveoli decreases, and an equilibrium is established between the partial pressure of the gas in the alveoli and that in the blood. When anesthesia is discontinued, a reverse process occurs, and at first there is rapid elimination of the anesthetic agent from the blood and the tissues into the alveoli of the lung. Gradually this is followed by slower elimination, as the concentration of the agent increases in the alveolar spaces. The importance of hyperventilation of the lungs with oxygen and then air at the termination of the period of administration of an anesthetic is apparent when one considers the mechanism of the diffusion of gases.

One must keep this physiologic process in mind when administering an inhalation anesthetic, because there are many factors which influence the diffusion of gas and vapors into the blood stream. The ultimate aim in administration of any anesthetic, especially an inhalation anesthetic, is the introduction of the agent into the tissues via the blood stream with the least possible disturbance to normal physiologic processes. Obstruction of the air passages or depression of breathing to such an extent that an adequate exchange of gases in the lungs is not possible definitely curtails the success of the anesthetic procedure. The difficulties most frequently encountered in relation to the maintenance of proper passage of air are those in which stridor (laryngeal spasm) occurs and those in which the tongue falls back against the posterior wall of the pharynx and obstructs the airway. The latter situation usually can be remedied by use of a mouth airway, a pharyngeal tube or an intratracheal tube. Stridor may occur as a result of administering an anesthetic agent too rapidly, and in such a case the stridor is usually due to the irritating action of the anesthetic on the vocal cords. Also, it may be attributable to indirect stimulation of other tissues, for example, traction on the pelvic and abdominal viscera.

The treatment of stridor due to too concentrated mixtures of anesthetic agents is usually simple and is accomplished by diluting the anesthetic vapor with oxygen. If stridor occurs when traction is made on viscera the situation is frequently more difficult to correct, and it is

usually embarrassing to the anesthetist. When visceral traction is made, laryngeal spasm may be produced in a patient under relatively deep as well as in one under light surgical anesthesia, and it seems that the most effective remedy is intratracheal intubation. Occasionally an increase in bag pressure helps to reduce the stridor and decrease the noise incident to vibration of the vocal cords. The difficulties encountered with this procedure are the possibility of distending the stomach with gas and the fact that the procedure is tedious and wasteful of gases. When an inhalation anesthetic is administered to a young child by the closed method (so-called carbon dioxide absorption method) one should employ a type of gas machine and carbon dioxide absorber unit which will require the least expenditure of respiratory effort on the part of the child. The 'to and fro' type of apparatus, with an absorber placed between a face mask and a breathing bag, probably requires less effort than the gas machines using so-called circle breathing units.

In the absence of respiratory obstruction there are certain other factors which influence physiologically the activity of respiration. These are chiefly of two types: chemical agents and afferent nerve impulses. Concerning the chemical stimuli of respiration, it is generally accepted that an increase in hydrogen ion concentration of the cell bodies of the formatio reticularis in the medulla enables these cells to emit more potent efferent nerve impulses. Although any acid, such as lactic acid, may increase the hydrogen ion concentration within these cells in the medulla and thus stimulate respiration under certain conditions, carbon dioxide has a specific affinity for these cells of the respiratory center, and any change in the p_H of blood effected by carbon dioxide seems to produce a greater respiratory response than an equivalent change produced by some other acid, such as lactic acid. A normal respiratory center is extremely sensitive to carbon dioxide, and the usual response of the center to carbon dioxide and oxygen is definite stimulation of respiration.

In the presence of narcosis and anoxemia with a diminished oxygen supply to the brain and medulla, the addition of carbon dioxide may cause a momentary stimulation of respiration. At the same time, however, it increases the demand of the center for oxygen, which is at a low level even prior to stimulation with carbon dioxide. The result is momentary respiratory stimulation followed suddenly by hypopnea and apnea. The only treatment for such a condition is administration of sufficient oxygen to rejuvenate the medullary center of the brain. If the cells of the respiratory center are severely depressed, either from narcosis or from anoxemia and have lost all their power of reacting to carbon dioxide the addition of this agent may cause a further narcotic action and respiration may cease after one or two breaths.

It is recognized also that anoxemia stimulates respiration, but its action is due to the production of certain afferent impulses with resultant reflexes around certain nerve receptors in the region of the carotid sinus and the ascending aorta. The general belief at present is not that anoxemia produces a direct stimulating effect on the respiratory center but rather that lack of oxygen in the cells of the respiratory center is a definite depressant.

The stimulus effected by anoxemia from the receptor in the region of the carotid sinus which causes hyperpnea is not mechanical as are the stimuli of some of the reflexes originating in this region which play a part in the control of pulse rate and blood pressure, rather it is a chemical stimulus. According to several investigators,¹ this reflex, originating from the carotid receptor in response to the stimuli of anoxemia, is more resistant than the reflex originating in the respiratory center to the deleterious effects of anesthetic agents, narcotic drugs, anoxemia and excessive concentration of carbon dioxide. Reflex stimulation of respiration by anoxemia must not be allowed to be present for any length of time, because irreparable damage may be done to the body tissues, especially those of the brain. Oxygen should be administered to abolish the anoxemia. Frequently, however, when oxygen is administered while respiration is being reflexly motivated by anoxemia, apnea or hypopnea will result, and clinically the picture is comparable to that observed when carbon dioxide has been administered. However, in spite of the apnea which may result, one must elect to remove the anoxemia and must not be misguided because respiration may have stopped momentarily. With the aid of artificial respiration plus oxygen, regular breathing usually will be resumed within a few minutes.

There is another neurogenic reflex which originates in the lungs, often referred to as the Hering-Breuer reflex, which regulates the rate and depth of inspiration by means of nerve impulses traversing the vagus nerve. This reflex is a check valve to limit inspiration or expiration and initiate a reflex either to distend or to deflate the lungs rhythmically. From a practical standpoint this reflex is most valuable when irritating vapors, such as those of ether, chloroform or diethyl ether, are employed in gaseous mixtures. As the concentration of ether is built up in the blood, the cells of the respiratory center become more narcotized, and it has been shown that the neurons responsible for initiation of expiratory efforts become depressed more quickly than do those associated with inspiratory activity. This is important because inspiratory movements of the chest disappear soon after expiratory

¹ Schmidt, C. F. Recent Studies on Some Physiological Phenomena Related to Anesthesia, Anesth. & Analg. **17** 24-34 (Jan-Feb) 1938

efforts are lost, and it is at this point that dangerous levels of anesthesia are reached and anoxemia ensues

It should be clear that the respiratory signs of anesthesia are tremendously important and deserve as much consideration as any one physical sign that may be demonstrated during inhalation anesthesia. Except in certain circumstances vasomotor and cardiovascular aberrations usually occur simultaneously with respiratory changes or inadequacies, and one should be alert to detect depressions in blood pressure, alterations in pulse rate and other signs of impending shock.

In the event of respiratory and circulatory depression during inhalation anesthesia, one should discontinue administration of anesthetics and ventilate the patient's lungs with oxygen either by manual compression with the use of the breathing bag or by means of slight puncture pressure with the aid of an intratracheal tube. The practice of simultaneously administering fluids intravenously when the systolic blood pressure is falling is almost unquestioned. Such an agent as saline solution, dextrose and saline solution, solution of acacia or whole blood should be used.

In many cases of impending shock, before capillary paralysis has occurred one finds a marked degree of vasoconstriction, because the vasomotor center is still active, at least for a time, until anoxemia supervenes and depresses the center. It is not wise to administer a vasoconstrictor agent, such as epinephrine, when the blood vessels are already markedly constricted. It is much more advantageous to restore the circulatory blood volume by means of intravenous administration of fluids, preferably blood, in order to insure a medium on which the heart can work. The opportune moment for the use of vasomotor agents occurs when the systolic blood pressure has not fallen to low levels that is, not below 70 or 80 mm of mercury. When vasoconstrictors are administered sufficiently early the vasomotor tone and the systolic pressure can be maintained for a reasonable time, at least long enough to permit relatively simple venipuncture.

There are many factors other than the anesthetic itself which influence or hasten so-called surgical shock, some of which are hemorrhage, loss of heat, sweating, trauma to tissues and duration of the surgical procedure. All these conditions should be considered during administration of the anesthetic, and it is advisable to synchronize the depth of anesthesia and specific supportive measures as far as possible with the physical status of the patient at varying intervals during the operation.

INTRA-ABDOMINAL PRESSURE

A CRITICAL REVIEW AND AN EXPERIMENTAL STUDY

CONRAD R LAM, MD

DETROIT

Previous writers¹ have commented on the confusion which exists on the subject of intra-abdominal pressure. The recent literature regarding this is small, but one finds many conflicting statements. Some writers state flatly that the intra-abdominal pressure is negative, others, that it is positive, atmospheric or variable. I cannot agree with the assertion in a recent paper² that "Several facts have been well established in the literature. There is normally a sub-atmospheric pressure within the peritoneal cavity." The authors of this paper used "intrapertoneal" and "intra-abdominal" interchangeably. In succeeding paragraphs it will be shown that it is not "well established in the literature" that the intra-abdominal pressure is negative and also that careful distinction must be made between the terms just referred to. The discrepancies in the literature are due to confusion in the use of these terms and to faulty interpretation of experimental results. The situation was well described by Livingston,^{1a} who stated "Authors, in describing conditions which prevail within limited regions of the abdomen or which exist in prescribed circumstances, have at times so extended their statements and so generalized, that considerable confusion and conflicting data have accumulated."

Is intra-abdominal pressure of sufficient significance to warrant careful definition and study? Surgeons have given adequate attention to blood pressure, intrapleural pressure, intrathecal pressure and various intravisceral pressures. In contrast, there is generally a poor conception of intra-abdominal pressure, although this pressure is probably significant in a fair number of conditions encountered clinically. For example,

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1 (a) Livingston, E M. A Clinical Study of the Abdominal Cavity and Peritoneum, *Am J Surg* 8 1110, 1930. (b) Hitzengerber, K. Zwerchfell und intraperitoneale Druck, *Klin Wchnschr* 8 961 (May 21) 1929. (c) Wildegren, H. Ueber den intraperitonealen Druck, *Mitt a d Grenzgeb d Med u Chir* 37 308, 1924.

2 Beecher, H K, Bradshaw, H H, and Lindskog, G. Effect of Laparotomy and Distention on Lung Volume, *J Thoracic Surg* 2 444 (June) 1933.

Brunn and Brill³ suggested that elevation of the diaphragm by postoperative distention might have an effect on pulmonary complications. Beecher, Bradshaw and Lindskog² found a decrease in pulmonary volume as a result of distention of the abdomen in experimental animals. Pneumoperitoneum is being used in selected cases of pulmonary tuberculosis as an adjunct to other forms of collapse therapy.⁴ Hernia, postoperative wound separation, ascites, ovarian cysts and parturition involve consideration of intra-abdominal pressure. These few examples are cited to justify this attempt to present an adequate conception of intra-abdominal pressure.

As has been stated, the terms intra-abdominal and intraperitoneal must be carefully distinguished in connection with this subject. Intra-abdominal pressure is a hydrostatic type of pressure, the result of the fact that the abdominal organs and other structures are contained in a vessel, the abdominal cavity. I accept Livingston's definition of "abdominal cavity": "The abdominal cavity is a term synonymous with the word abdomen. Within the cavity are situated all of the abdominal organs, namely, most of the alimentary canal, the digestive glands, kidneys, ureters, part of the bladder, peritoneum, blood vessels, nerves and certain fetal remnants." Except for the pelvic outlet, the abdominal cavity is a space enclosed by structures resistant to pressure, namely, bones, muscles and fascia. The retroperitoneal structures are affected by changes in abdominal tension as much as are the so-called intraperitoneal structures. For example, urine may flow from the ureteral orifices in spurts synchronous with the respiratory fluctuations in intra-abdominal pressure. Since pressures are freely transmitted from the abdomen to the true pelvis, the latter will be considered as an extension of the former, and most general statements regarding pressure apply to both cavities.

To clarify my conception of intra-abdominal, intraperitoneal and intravisceral pressures, a mechanical model of the abdomen was constructed, a cross section of which is shown in figure 1. Coils of thin rubber tubing (surgical drains) were placed inside a "peritoneal cavity" which consisted of a bag of transparent rubber sheeting. A small hydrostatic bag (A) was inserted between the "intestines" and the

³ Brunn, H., and Brill, S. Postoperative Atelectasis. Factors in Etiology, Prevention and Treatment, *Tr. Am. S. A.* **48** 53, 1930.

⁴ Banai, A. L. Observations on the Radiological Chest Volume During Artificial Pneumoperitoneum Treatment, *Radiology* **31** 48 (Jul.) 1938. Trimble, H. G. Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis. *Dis. of Chest* **4** 18 (June) 1938. Hobbs, A. W. Pneumoperitoneum, an Adjunct to the Treatment of Pulmonary Tuberculosis, *ibid.* **4** 18 (Sept.) 1938. Stokes, J. B. Pneumoperitoneum for Pulmonary Compression, *Illinois M. J.* **73** 137 (Feb.) 1938.

"abdominal wall" The coils of tubing (*B*) were inflated with a bulb. The pressures in spaces *A*, *B* and *C* were recorded on a kymographic drum.

At the start of the experiment, the "intestines" were in a flattened condition, and the excess air in the peritoneal space was removed, it being borne in mind that the true peritoneal space is only a potential one. The coils of tubing were then inflated until a high "intravisceral" pressure was obtained. This procedure caused the bag which measured intra-abdominal pressure to indicate an increase, but the pressure in the intra-

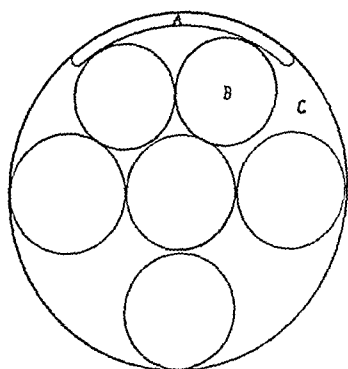


Fig 1—Diagram of a mechanical model of the abdomen. *A*, intra-abdominal pressure, *B*, intravisceral pressure, *C*, intraperitoneal pressure.

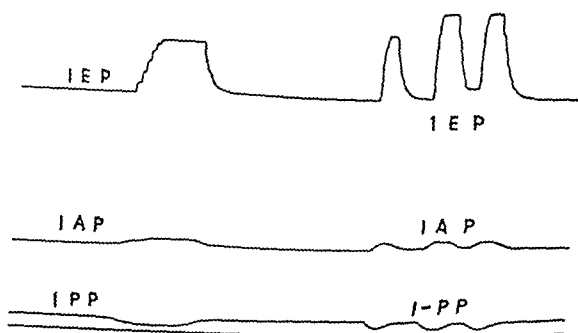


Fig 2—Kymographic record of pressures in the mechanical model. *I-E P*, intraenteric (intravisceral) pressure, *I-A P*, intra-abdominal pressure, *I-P P*, intraperitoneal pressure.

peritoneal space showed no increase, on the contrary, there was a paradoxical fall. This was obviously due to the fact that in the change of the "intestines" from the flattened condition to the distended, cylindric condition there was an increase in the potential intraperitoneal space, and a negative pressure was created. A record of the paradoxical behavior of the "intraperitoneal" pressure is shown in figure 2.

In the review of the literature which follows it will be seen that the investigators fall into two classes (1) those who tried to determine

intra-abdominal pressure (*A*, fig 1) by measuring intravisceral pressure (*B*), and (2) those who measured intraperitoneal pressure (*C*)

1 In this class are those who placed bags in the stomach, urinary bladder, rectum and uterus. Obviously it is impossible to eliminate entirely the intrinsic pressure of the viscus due to the tonicity or contractions of its walls. Certain of the results would appear to be valid and these instances will be mentioned in the review which follows.

2 In this class are those who made manometric measurements of the intraperitoneal pressure by placing needles or trocars in the peritoneal space. This method is subject to the following limitations. If positive pressure exists it is not reflected by the manometer because of the lack of a medium to transmit the pressure. If atmospheric pressure exists it cannot be distinguished from positive pressure. If negative pressure exists, this is correctly registered on the manometer. However, as was demonstrated with the mechanical model, it is theoretically possible to obtain negative intraperitoneal pressure in the presence of positive intra-abdominal pressure.

For a review of the literature up to 1911, dependence has been placed on the extensive bibliography of Emerson⁵. He cited 4 authors who stated that the intra-abdominal pressure is atmospheric, 6 who stated that it is negative, 12 who stated that it is positive and 5 who stated that it is variable. The paper of Emerson and subsequent papers will be reviewed briefly.

Emerson did 24 experiments, inserting a trocar attached to a water manometer into the peritoneal cavities of various experimental animals. He concluded that the normal intra-abdominal pressure is slightly positive. His twenty-fifth and last experiment was as follows: a laparotomy was done on a dog under water, an inverted bell jar filled with water being held over the operative site to catch any bubbles of gas which might escape from the peritoneal cavity. No bubbles escaped and he rightly concluded that there is normally no gas in the peritoneal cavity. However, his last experiment casts doubt on the interpretation of the results obtained in the previous 24, because in the absence of a gaseous medium to flow out of the manometer system the positive pressure readings must have been artefacts.

The work of Keppich⁶ (1921) is often cited. This author cautioned against confusion of intra-abdominal and intravisceral pressures but he used the terms intraperitoneal and intra-abdominal interchangeably. He put a tenestrated needle in the peritoneal cavities of dogs and human

⁵ Emerson H. Intra-Abdominal Pressures, *Arch Int Med* 7:755 (June) 1911.

⁶ Keppich J. Ueber den intraperitonealen Druck. *Arch i klin Chir* 116:276 (July 30) 1921.

beings. He concluded that the normal intraperitoneal pressure in man is -0.5 to -3.4 cm of water. He noted that manual compression of the abdomen, coughing and changes of position did not alter the pressure. His results gave no information about intra-abdominal pressure, for the reasons stated.

The next paper is that of Wildegans^{1c} (1924). He inserted a needle in the peritoneal cavities of 60 patients. In 19 of these the puncture was in the epigastrium, and in 41 it was in the hypochondrium. In 56 instances there was no fluctuation of the manometer. In 3 there was a positive reading, and in these there was gas or fluid in the peritoneal space (bullet wound, perforated ulcer and ascites). In 1 instance a negative pressure was registered, but only during inspiratory dyspnea while an anesthetic was being given. Wildegans then attempted to measure the intra-abdominal pressure by measuring the force required to introduce air into the peritoneal cavity. By this method he found a positive pressure of 4 cm of water in rabbits and pressures of 1.5 to 12 cm in 46 human beings. The subjects were all in the horizontal position, and the punctures were made near the umbilicus.

The other author who is often cited in support of the statement that the intra-abdominal pressure is negative is Wagoner.⁷ Monkeys, rabbits, cats and dogs were placed in the supine position, and a needle connected with a manometer was thrust into the peritoneal cavity. Slightly negative pressures were encountered, which fluctuated with respiration. Normal values for monkeys were said to be -0.2 to -0.4 cm, for rabbits, -3.0 to -5.5 cm, for cats, -0.8 to -1.4 cm and for dogs, -2.0 to -4.4 cm. Fifty cadavers were tested, and an average value of -5 cm was obtained. Positive pressures were obtained in 9 cases, associated with distention, obesity or ascites. It is unnecessary to point out again the shortcomings of this method of determining intra-abdominal pressure.

Overholt⁸ recognized the fact that the peritoneal cavity is a cleft, empty except for a thin coating of fluid. However, he accepted the work of Keppich and that of Wagoner and, looking for a negative pressure, inserted cannulas into the peritoneal cavity in the region of the epigastrium and measured the intraperitoneal pressure with the closed manometer of Lewis. A mean subatmospheric pressure was recorded for 32 dogs, and 1 animal showed an atmospheric pressure. The values ranged from -0.5 to -10 cm. A shift to the vertical position with the head up caused a marked fall in the pressure in the upper part of the abdomen and an increase in pressure in the lower part.

⁷ Wagoner, G. W. Studies on Intra-Abdominal Pressure, *Am J M Sc* 171: 697 (May) 1926.

⁸ Overholt, R. H. Intra-Peritoneal Pressure, *Arch Surg* 22: 691 (Mar) 1931.

Murphy and Mengert⁹ placed a balloon in the vagina and, checking the position roentgenographically, found that the top of the balloon was out of the true pelvis. They tested the effect of visceral weight and found that it varied from atmospheric with the subject in the knee-chest position to 31.2 cm of water with the subject in the sitting position. They found that voluntary straining produced the maximum effect in the sitting position, a pressure of 200 cm of water being obtained.

Salkin¹⁰ repeated some of the work of Wagoner with similar results. Kountz, Gottlieb and King¹¹ placed a bag in the stomach of a dog. They obtained values ranging from atmospheric to —4 cm of water. With cough, the pressure went up to 40 cm of water.

It is seen that in the previous experimental work attempts have been made to measure intra-abdominal pressure (*A*, fig 1) by measuring *B* or *C*. The question which presents itself is, Why not measure *A* directly? A small bag placed in the abdominal cavity could be used to measure the effective intra-abdominal pressure at any given point in the abdomen. There are two objections. First, the hermetic conditions of the peritoneal cavity have been disturbed by the operation of inserting the bag, and air has been permitted to enter. Second, a foreign body has been introduced. The first objection can be partly disposed of by assuming that the air introduced at laparotomy may be largely removed by subsequent needle aspiration and that what remains may be absorbed shortly. The second objection is valid, and it can only be stated that the pressure determinations in the experiments to be described are for recently laparotomized dogs with a small foreign body left in the abdominal cavity.

EXPERIMENTAL METHOD AND RESULTS

The intra-abdominal pressure in dogs was measured by inserting a small rubber bag (glove finger) in various parts of the abdominal cavity. The bag was connected to a water manometer by means of a small rigid rubber tube (no 10 catheter). The bag held about 7 cc of air without the development of intrinsic pressure. When a determination of pressure was to be made the bag was emptied by suction and partially inflated with 4 cc of air, after which connection with the manometer was made. Thus, both positive and negative pressures were indicated. The intra-abdominal pressure was varied by inflation of the alimentary tract.

⁹ Murphy, D P, and Mengert, W F. Intra-Abdominal Pressures Created by Voluntary Muscular Effort. I. Technique of Measurement by Vaginal Balloon, *Surg, Gynec & Obst* **57** 487 (Oct) 1933. Mengert, W F, and Murphy, D P. Intra-Abdominal Pressures Created by Muscular Effort. II. Relation to Posture in Labor, *ibid* **57** 745 (Dec) 1933.

¹⁰ Salkin D. Intra-Abdominal Pressure and Its Regulation, *Am Rev Tuberc* **30** 436 (Oct) 1934.

¹¹ Kountz, W B, Gottlieb, L, and King R. The Influence of Changes of Abdominal Tension upon Pulmonary Function. *J Clin Investigation* **15** 601 (Nov) 1936.

with air, by ciation of a tension pneumoperitoneum and by changing the position of the animal The intraperitoneal pressure was frequently measured by thrusting a large needle into the peritoneal cavity, to demonstrate the futility of this method of determining intra-abdominal pressure

EXPERIMENT 1 (to determine the effect of distention of the alimentary tract on intra-abdominal and intraperitoneal pressure) —On March 10, 1939, an experiment was performed on a bitch weighing 10 Kg with the animal supine, the intraperitoneal pressure was atmospheric in both hypochondriac regions The intrapleural pressure was —1 to —5 cm of water The animal was anesthetized with 6 cc of dial administered intraperitoneally A short incision was made in the midline above the umbilicus The lower part of the colon was ligated, and a hydrostatic bag was inserted in the epigastric region The incision was closed, and the air in the peritoneal cavity was removed by aspiration A cannula was

TABLE 1—Results of Experiment 1

Intravisceral Pressure, Cm of Water	Intra Abdominal Pressure, Cm of Water	Intraperitoneal Pressure
Before inflation	10	0 (atmospheric)
During inflation {	11	0
	23	0
	30	0

TABLE 2—Results of Experiment 2

Intraperitoneal Pressure (Tension Pneumoperitoneum), Cm of Water	Intra Abdominal Pressure, Cm of Water
0	4
4	11
10	14
15	16.5
20	20
0	4.5

inserted in the esophagus for subsequent inflation of the alimentary tract The results in this experiment are shown in table 1

EXPERIMENT 2 (to determine the effect of tension pneumoperitoneum on intra-abdominal pressure) —The air in the alimentary tract of the same animal was removed, and various degrees of tension pneumoperitoneum were created (table 2)

Experiment 1 showed that moderate distention did not produce a significant rise in the intra-abdominal pressure, but higher intravisceral pressure (up to 40 cm of water) caused an increase The insertion of a needle into the intraperitoneal space gave no indication of the elevated intra-abdominal pressure The experiment with tension pneumoperitoneum showed that the pressure of the air was added to that due to the weight of the viscera until a pressure of 20 cm water was reached, after which the intraperitoneal and intra-abdominal pressures were identical

EXPERIMENT 3 (to determine the abdominal pressure in various parts of the abdomen and the effect of change of posture) —On April 10, 1939, a dog weighing 10 Kg was anesthetized with 6 cc of dial given intraperitoneally The intrapleural pressure was —1 to —10 cm of water The intraperitoneal pressure in the

epigastrium with the animal supine was -0.5 cm of water. With the animal erect, the intraperitoneal pressure under the diaphragm fluctuated between -4 and -6 cm. An incision was made in the midline above the umbilicus. One pressure bag was sutured to the central tendon of diaphragm, and another was attached to the anterior abdominal wall, just above the bladder. The pressures on the two bags

TABLE 3—Results of Experiment 3

Position of Animal	Intra Abdominal Pressure Cm of Water		
	Under Diaphragm		In Lower Part of Abdomen
	On Inspi ration	On Expi ration	
Supine	3.0	3.5	5.5
Erect	-3.5	-3.0	10.0
Head down	11.0	16.0	0.5
Head up (45 degrees)	-2.5	-2.0	8.0
Head down (45 degrees)	6.0	5.5	2.0
Supine (second reading)	3.0	3.5	5.5

TABLE 4—Results of an Additional Experiment *

Position of Animal	Intra Abdominal Pressure Cm of Water		
	Under Diaphragm		In Lower Part of Abdomen
	On Inspiration	On Expiration	
Supine	8.0	9.0	9.0
Head up	2.0	5.0	12.0
Head down	17.0	19.0	2.0

* May 5 1939. The animal was a bitch weighing 6 Kg. Ether anesthesia was used. The subject had recovered from the anesthesia when the readings were made.

TABLE 5—Result of a Second Additional Experiment *

Position of Animal	Intra Abdominal Pressure Cm of Water		
	Under Diaphragm		In Lower Part of Abdomen
	On Inspiration	On Expiration	
Supine	1.0	-4.0	4
Head up	-5.0	-2.0	6.10 (Insp Exp)
Head down	10.5	7.5	0.5

May 8 1939. The animal was a bitch weighing 6.5 Kg. Ether anesthesia was used and narcosis was obtained with $\frac{1}{2}$ grain (0.03 Gm.) of morphine.

with the animal in various positions were noted (table 3). (Similar experiments were performed on 5 additional animals; the results in 2 other typical experiments being recorded in tables 4 and 5.)

COMMENT

In these experiments an attempt has been made to demonstrate that abdominal pressure is a function of the hydrostatic pressure of the viscera and the relation of the volume of the abdominal cavity to the

volume of its contents. Increase in the volume of the alimentary canal by distention makes the abdominal contents relatively large for the abdominal cavity, and increase in pressure results. In this connection it should be mentioned that considerable increase in the volume of the abdominal contents is tolerated before tension develops, because of reflex relaxation of the abdominal wall as demonstrated by Coombes¹². Spasm of the abdominal muscles or voluntary straining for any reason tends to decrease the size of the abdominal cavity and thus to raise the pressure. When the animals were held in an upright position, a negative pressure was usually found under the diaphragm, but in the case of 1 animal (table 4), which had recovered from the anesthetic and was straining, a positive pressure was maintained.

It is evident that concise statements may be made about abdominal pressure if such statements are qualified by naming the exact region of the abdomen under consideration and the posture of the body. For example, the statement "The intra-abdominal pressure was positive" is meaningless, while the statement "With the subject standing, the intra-abdominal pressure at the left internal abdominal ring was 25 cm of water" is significant.

In this study no direct measurements of the intra-abdominal pressure in man have been made. On the basis of these animal experiments and the work of others⁹ on man it is probable that in an adult subject in the standing position there is a pressure of 25 to 40 cm of water in the lower part of the abdomen and in the pelvis. If the abdominal muscles are under tension, higher values are reached. This pressure decreases as the upper part of the abdomen is approached, until under the dome of the diaphragm there may be a negative pressure. This is variable, depending on the tonicity of the abdominal wall, and it shows respiratory fluctuation. Some observers¹³ have noted pressures in this locality identical with the intrapleural pressure.

If the subject is standing on his head, the pressure relations are reversed, a positive pressure being against the diaphragm and a negative pressure in the pelvis. This is illustrated by the ballooning of the rectum and bladder when the subject is in the knee-chest position.

SUMMARY

1 The literature on the subject of intra-abdominal pressure is reviewed, and the reasons for many conflicting opinions are indicated.

12 Coombes, H. C. The Mechanism of Regulation of Intra-Abdominal Pressure, *Am J Physiol* **61** 159 (June) 1922.

13 Hamilton, C. E., and Amazon, P. Accidental Pneumoperitoneum in Artificial Pneumothorax Therapy, *Am Rev Tuberc* **34** 160 (Oct) 1936.

2 A plea is made for exact terminology in statements regarding intra-abdominal pressure. The importance of distinguishing between intra-peritoneal, intravisceral and intra-abdominal pressures is emphasized. Statements should be qualified by mentioning the exact region of the abdomen under consideration and also the posture of the body.

3 Experiments are described in which the intra-abdominal pressure in various regions of the dog's abdomen under different conditions was determined by the use of a small hydrostatic bag.

4 Statements are made regarding the probable pressure relations in the human abdomen.

THE APPENDICAL STUMP

ITS MANNER OF HEALING IN THE OPEN AND IN THE CLOSED METHOD OF TREATMENT

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The technic of operations in all fields of surgery has been standardized on physiologic principles so that, while the detailed procedure itself may and does vary with different surgeons, the underlying principle on which the procedure is based is the same. There is, however, an outstanding exception, and that applies to treatment of the stump of the appendix. While methods of handling the stump are fairly numerous, they may all be grouped into two categories: (1) the buried stump method and (2) the nonburied stump method.

Frequently the reasons brought forward by the proponents of one method in justification of their procedure are the very ones that are used by the opponents of that same method in justification of the other. For instance, Torek¹ pointed to the danger of postoperative adhesions and intestinal obstruction in cases in which simple ligation or the unburied stump method was used and cited evidence to prove that this danger is real. In 1 instance a typical picture of acute intestinal obstruction occurred six weeks after an appendectomy performed by the simple ligation method. The patient died without being operated on, and at autopsy the stump of the appendix was seen to be adherent to the parietal peritoneum, with a loop of intestine caught and obstructed beneath it. In a second case cited by Torek the patient was operated on for acute ileus that occurred after a similar operation, and the findings were the same.

Hortolomei,² on the other hand, reported the cases of 2 patients who had been operated on by the buried stump method and in whom acute intestinal obstruction did occur postoperatively. In both patients adhesions were found at the site of the appendical stump. This author maintained that the buried stump causes formation of an abscess, which

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Read before the Surgical Section of the New York Academy of Medicine on April 7, 1939.

1 Torek, F. *Zentralbl. f. Chir.* **59** 204, 1932.

2 Hortolomei, N. *Zentralbl. f. Chir.* **58** 2379, 1931.

may rupture either into the intestinal lumen or within the general peritoneal cavity in the second instance causing general peritonitis. He cited the history of such a case, in which the appendical stump was buried and the patient had some pain in the right lower quadrant of the abdomen on the fourth postoperative day. At reoperation peritonitis was found, originating from a ruptured abscess that had formed at the site of the appendical stump. Hortolomei performed "simple ligation appendectomy" on 621 patients without any accidents (except for 1 death from embolism on the eighth postoperative day), and in 13 of these whose condition subsequently required a second laparotomy he found a total absence of adhesions. He cited de Martel, who reported 3 cases of generalized peritonitis following treatment by the buried stump method as a result of perforation of the cecal wall by the purse string suture. De Martel³ reported the findings in 61 cases in which a second laparotomy was performed on patients who had been operated on for appendicitis by the open method. In none of these did he find any evidence of postoperative adhesions. Hilarowicz⁴ reported a case of appendicitis in which simple ligation was employed in the treatment of the stump and in which peritonitis set in on the third and the patient died on the fifth postoperative day. Autopsy showed generalized peritonitis, with the appendical stump completely patent.

Roeder⁵ reported his findings in 105 laparotomies performed on appendectomized patients. In 98 cases he found adhesions. In 8 cases he considered these of no significance. In the remaining 90, however, he considered them "of a type (1) to cause an interference with the peristalsis of the caecum, (2) to cause localized pain and tenderness and (3) to be looked on as a potential point of small bowel obstruction." This author maintained that "the two most overlooked factors in the etiology of crippling post-operative adhesions are the purse-string inverting suture and the neglected stump of the meso-appendix" and that "the most frequent source of infection is the suture used to invert the stump of the appendix."

Maloney,⁶ in a report of 3,500 cases in which the simple ligation method was used and the stump left unburied, stated that he encountered no postoperative ileus and that in the cases in which subsequent reoperation was done adhesions were never found. Riedel⁷ stated significantly

I consider the suturing of a peritoneal cuff over the appendix stump as a very dangerous procedure. As regards going so far as to bury the infected stump into the caecal wall this must absolutely lead to perforation into the lumen or

3 de Martel F. Bull. et mem. Soc. de chir. de Paris **46** 1438, 1920.

4 Hilarowicz H. Zentralbl. f. Chir. **59** 2407, 1932.

5 Roeder C. A. Appendectomy. A Study in Technique. Arch. Surg. **11** 18 (July) 1925.

6 Maloney F. F. Ann. Surg. **82** 260 1925.

7 Riedel G. Zentralbl. f. Chir. **30** 1393 1903.

the caecum. If the inverting sutures hold and adhesions are strong enough, *we will not fear an intraperitoneal rupture*, but need only consider the disadvantages resulting from an ulcer in the caecum as a result of the intracaecal rupture.

Mayo,⁸ in a publication entitled "Appendicitis," stated

There are four reasons why I do not invert the carbolized stump of the appendix. (1) Dr Robertson of the Section on Pathologic Anatomy at the Clinic has found that invariably, in cases in which appendectomy with inversion of the stump has been done in combination with some other surgical procedure and death has resulted, there is a pus pocket in the inverted stump up to twenty-one days postoperatively, (2) the cultured suture material used to invert the stump, once having run through the intestinal wall, invariably is infected with pathogenic bacteria, (3) noninversion shortens the surgical procedure, and (4) I have not had occasion to regret not having inverted the stump.

Hermann⁹ reported a case in which operation was done by the buried stump method and in which five days after the operation an abscess formed within the cecal wall, perforated into the peritoneal cavity and caused death. Burkle-de le Camp,¹⁰ from Lexer's clinic, reported the end results in 3,200 cases of acute and chronic appendicitis treated by inversion of the open stump. He claimed to have avoided necrosis, abscess formation, fecal fistula and hemorrhage. Fowler,¹¹ however, called attention to the danger of secondary hemorrhage from an artery that is found fairly frequently running longitudinally within the wall of the appendix. Seelig¹² called attention to this same complication, which was described to him in a communication from Dr Charles Elsberg and Dr Charles Mayo. Lilienthal¹³ thirty-six years ago strongly advocated simple ligation as the safest and most effective method and noted an entire absence of adhesions in all cases in which he performed a laparotomy on an appendectomized patient.

In spite of all the evidence favoring the open method, the closed, or buried stump, method still is used most extensively. With such strongly divided and antithetic opinions regarding the proper method of treating the appendical stump, it seemed to me worth while to determine what actually happens in the experimental animal when the stump is treated by the open method in one series of animals and by the closed method in a second series.

MATERIAL AND METHOD

The adult rabbit was used in these experiments. In all there were 23 experiments with the buried stump method and 16 with simple ligation. About 3 to 4

8 Mayo, C W. Southwest Med **18** 397, 1934.

9 Hermann, F. Zentralbl f Chir **28** 1028, 1901.

10 Burkle-de le Camp, H. Zentralbl f Chir **59** 2082, 1932.

11 Fowler, H. Am J M Sc **113** 152, 1897.

12 Seelig, M G. Ann Surg **40** 710, 1904.

13 Lilienthal, H. M News **83** 1020, 1903.

inches (7.5 to 10 cm.) of the appendix was amputated after simple ligation of the appendix proper. In one series of animals the stump was inverted and buried. In the other series the stump was dropped, untreated, into the free peritoneal cavity. At varying intervals after operation the animal was anesthetized and the appendical stump first examined *in situ* and then removed for microscopic examination. In the first 8 experiments to be reported in detail, the stump was treated by simple ligation, in the remainder, it was inverted and buried.

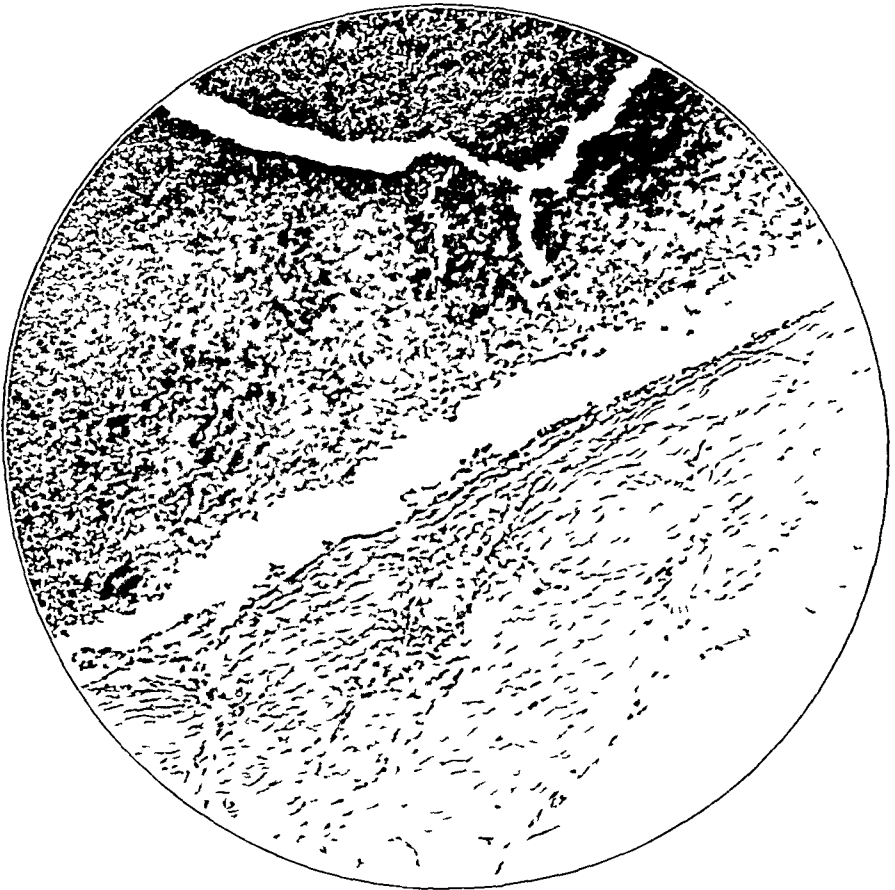


Fig 1 (rabbit 3) —Section of an appendical stump treated by simple ligation. The photomicrograph was taken fourteen days after the operation.

PROTOCOLS

RABBIT 1 (examined at three months) —There was no evidence of any appendical stump. The intestine was adherent to the former site of the stump.

RABBIT 2 (examined at ninety-two days) —The stump of the appendix was free. The surface was smooth internally and externally. Microscopic examination showed the mucosal layer to be continuous. The muscle layer was united by young connective tissue with numerous mitotic figures.

RABBIT 3 (examined at fourteen days) —The stump appeared as a gray-white globular mass covered with a thin, glistening membrane. Microscopic examination showed complete reproduction of the blind extremity with its mucosa. The stump proper was surrounded by young connective tissue and was completely necrotic.

RABBIT 4 (examined at nine days) —Omentum completely surrounded the stump. Microscopic examination showed the stump completely necrotic and surrounded by young connective tissue which separated it from the distal portion of the cecum.



Fig 2 (rabbit 9) —Section of a buried appendical stump. The photomicrograph was taken one day after the operation.

RABBIT 5 (examined at five days) —The stump was covered with omentum. The blind extremity was reformed. Young connective tissue could be seen uniting the muscle tissue. The stump proper was completely necrotic; there was aseptic necrosis in different stages. The necrotic stump was completely surrounded by new connective tissue.

RABBIT 6 (examined at fifty days) —The stump consisted of a small piece of an ovoid mass completely covered with glistening peritoneum. The mucosal lining of the appendix proper was normal throughout.

RABBIT 7 (examined at three days) —The stump was small, grayish white and sharply demarcated. There was massive necrosis of the stump.

RABBIT 8 (examined at twenty-nine days) —There was a small white appendical stump. There was no sign of inflammation. The mucous membrane layer of the blind extremity was continuous throughout.

RABBIT 9 —On Sept 17, 1934, the appendix was ligated and amputated 4 inches (10 cm) from the tip with a catgut ligature. The stump was inverted with a

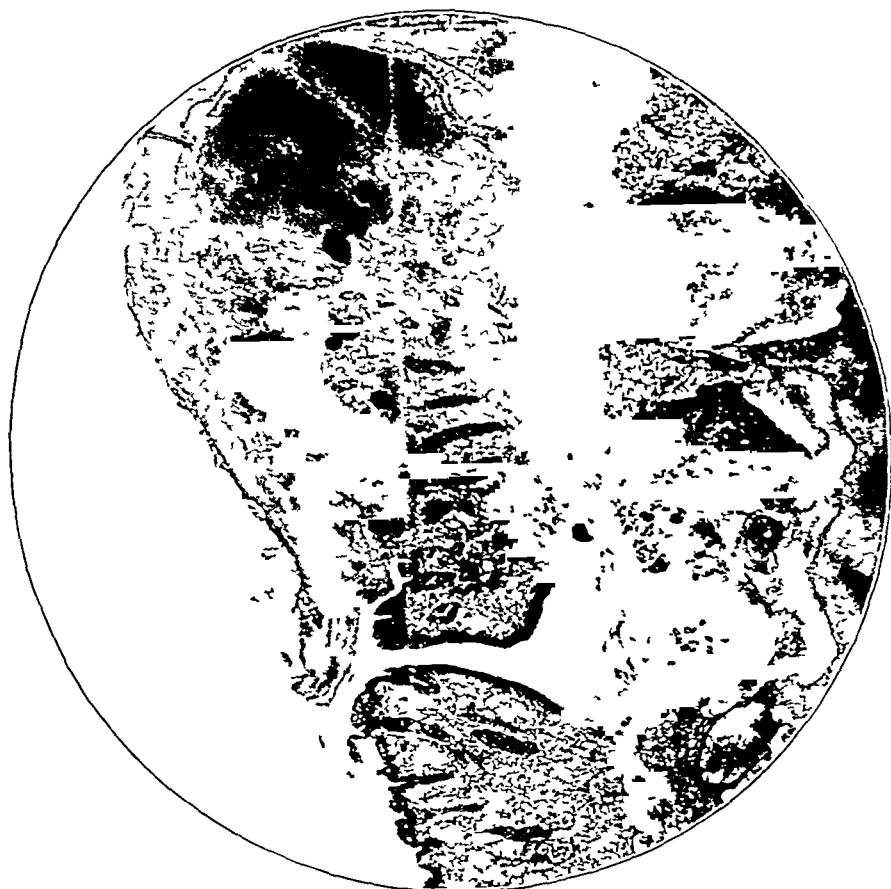


Fig 3 (rabbit 9) —Another section of the same buried stump

silk purse string suture. On the next day (September 18) the animal was killed. The appendical stump was adherent to a loop of small intestine. About $\frac{1}{16}$ inch (0.16 cm) from the site of adhesion there was seen a horizontal red-blue streak $\frac{1}{16}$ inch (0.16 cm) wide and $\frac{3}{8}$ inch (1.1 cm) long. On inversion of the stump there was noted on the mucosal surface at the tip an area about $\frac{1}{16}$ inch (0.16 cm) in diameter, gray and sharply outlined. Microscopic examination revealed a marked inflammatory reaction within the tissues of the buried stump and necrosis involving the distal mucosa with ulceration into the free lumen of the cecum. The tissues at this site showed hemorrhagic infiltration.

RABBIT 10—On Sept 28, 1934, the appendix was ligated and amputated about 3 inches (7.5 cm) from the tip. The stump was inverted with a silk purse string suture. On October 3 the animal was killed. The stump of the appendix was firmly adherent to two loops of small intestine. The lymph nodes in the mesentery were enlarged and soft. On inversion of the appendical stump, the mucosa of the distal pole was seen, it was brown and sharply limited from the surrounding normal-appearing mucosa. When part of this discolored tissue was teased out, it proved to be necrotic. This area was about $\frac{1}{2}$ inch (1.3 cm) in diameter. Microscopic examination revealed typical necrotic changes in the discolored area. The mucosa at this site was completely ulcerated, giving the necrotic tissue direct approach to the lumen of the intestine. The surrounding tissue contained hemorrhagic infiltration.

RABBIT 11—On Sept 7, 1934, the appendix was ligated and amputated about 2 inches (5 cm) from the tip with catgut. The stump was inverted with a silk purse string suture.

On September 12 the animal was killed. The stump of the appendix was adherent to the lateral wall of the ascending colon. About $\frac{1}{4}$ inch (0.6 cm)

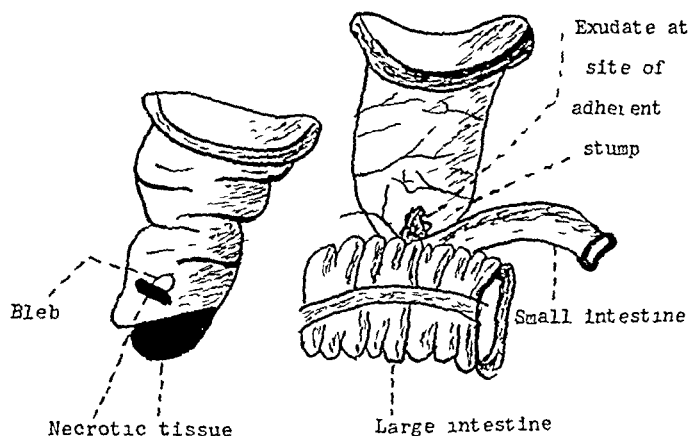


Fig 4 (rabbit 11)—Inverted appendical stump five days after the operation

from the purse string suture there was an irregular patch of gray-white exudate. Behind the colon there was seen a loop of small intestine adherent to the stump. These three structures were excised en masse.

When the appendical stump was inverted and turned inside out it was clearly seen that the lowermost portion consisted of a brown structure about $\frac{1}{2}$ inch (1.3 cm) in diameter, it was sharply delimited from the rest of the specimen, which was perfectly normal in appearance. A similar brown area about $\frac{1}{8}$ inch (0.3 cm) in diameter was seen to be separated from the first brown area by a zone of healthy mucosa $\frac{1}{4}$ inch (0.6 cm) wide. Part of this second discolored area was loosened from the underlying tissue, which consisted of a superficial yellow-based ulcer. The mucous membrane over the discolored area on microscopic examination showed complete necrosis of tissue, vacuolation, pyknosis and shadow cell formation. The immediately adjacent tissue showed a marked inflammatory reaction. The rest of the mucosa was normal in appearance.

RABBIT 12—On Oct 8, 1934, the appendix was ligated and amputated about $3\frac{1}{2}$ inches (8.8 cm) from the tip. The stump was inverted with a silk purse string suture. On October 15 the animal was killed. The appendical stump was adherent to the small bowel. The mesenteric glands were enlarged and soft. On

inversion of the appendical stump a circular area at the extreme tip, about 1 cm in diameter, was seen sharply delimited from the surrounding normal-appearing mucosa. This area was dark brown. At one portion of this area a piece of the silk purse string suture could be seen.

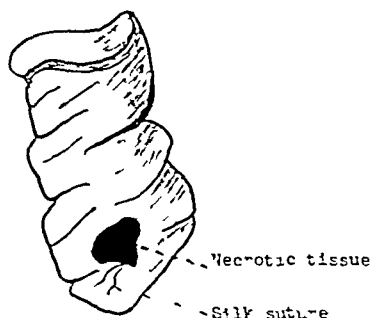


Fig 5 (rabbit 12) —Inverted appendical stump seven days after the operation

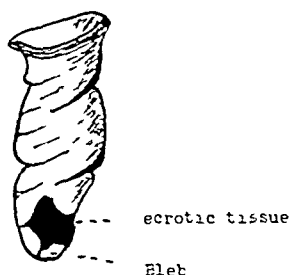


Fig 6 (rabbit 13) —Inverted appendical stump four days after the operation

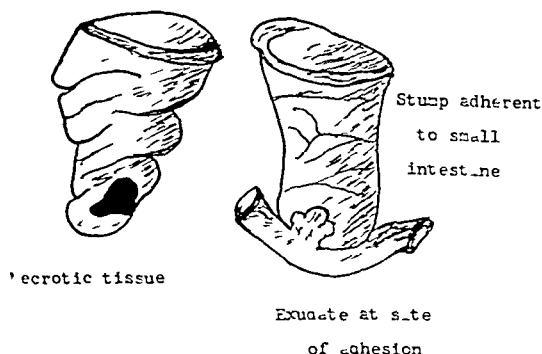


Fig 7 (rabbit 14) —Inverted appendical stump nine days after the operation

Microscopic examination disclosed complete necrosis of the discolored area. The soft tissues surrounding it presented marked hemorrhagic infiltration and the mucosa overlying the necrotic area was ulcerated yielding direct access of the necrotic tissue to the lumen of the intestine.

RABBIT 13—On Sept 14, 1934, the appendix was ligated and amputated 4 inches (10.1 cm) from the tip. The stump was inverted with a silk purse string suture. On September 18 the animal was killed. The appendical stump was adherent to the small intestine. (The appendix and the adherent portions of small intestine had been removed en masse for microscopic examination.) The mesenteric glands were soft and enlarged. The inverted appendical stump presented an irregularly circular area about $\frac{1}{2}$ inch (1.2 cm) in diameter, sharply limited

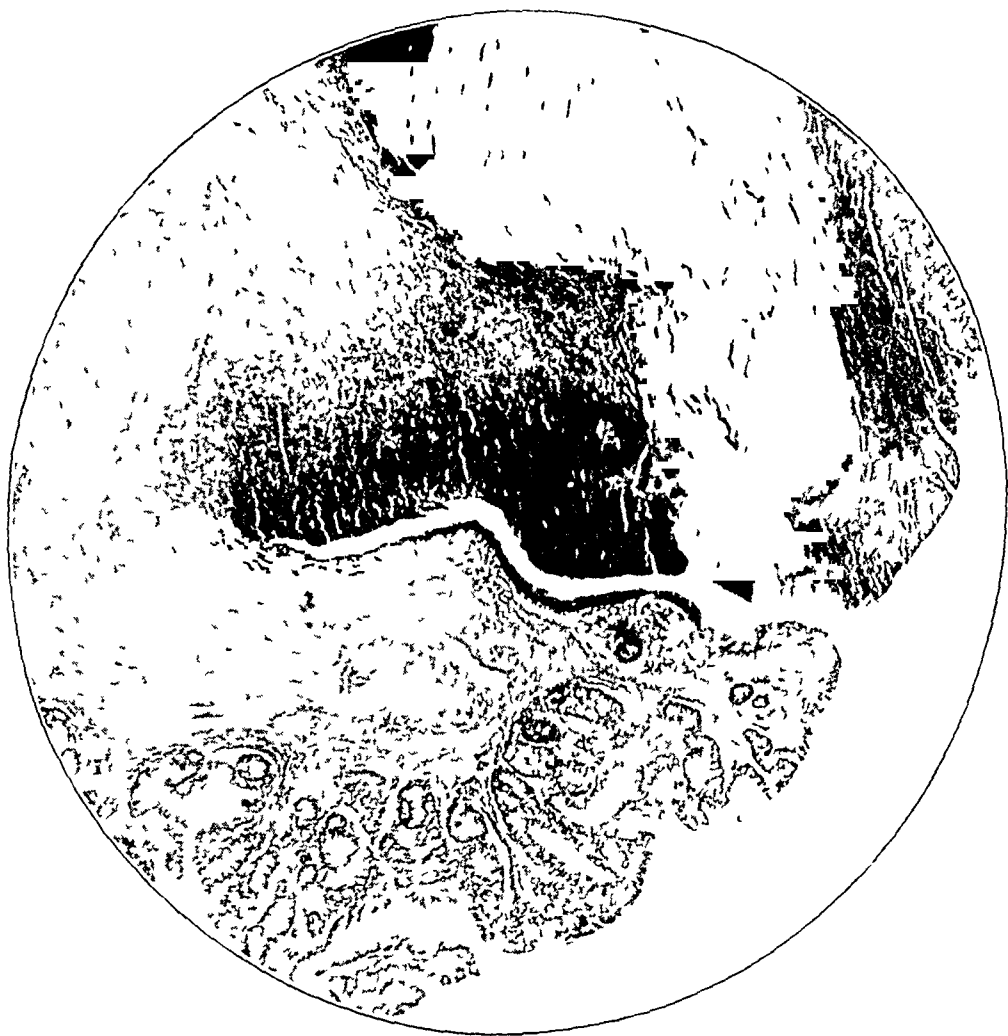


Fig 8 (rabbit 14)—Section of a buried appendical stump. The photograph was taken nine days after the operation.

and gray-brown, situated near the distal blind extremity. Immediately distal and adjacent to the brown area were two small blebs about $\frac{1}{16}$ inch (0.16 cm) in diameter. The mucosa of the ulcerated areas on microscopic examination showed complete necrosis, with direct access to the lumen of cecum. The adjacent mucosa showed a marked inflammatory reaction, with a submucous hemorrhagic infiltration.

RABBIT 14—On Sept 12, 1934, the appendix was ligated and amputated about 2 inches (5 cm) from the distal extremity with catgut. The stump was inverted with a silk purse string suture. On September 21 the animal was killed. The

of the appendix was found adherent to the small intestine. The silk suture was partly buried beneath the adhesion. A group of coalescent gray-white areas about $\frac{1}{2}$ inch (1.3 cm) in diameter could be seen at this adherent zone. These areas were subperitoneal and slightly elevated. The mesenteric glands were soft and large. The inverted specimen showed two discrete oval ulcerations filled with gray-brown substance which in one of the ulcers had a frayed-out appearance. These areas were $\frac{1}{16}$ to $\frac{1}{8}$ inch (0.16 to 0.3 cm) in diameter. The rest of the mucosa was normal in appearance. Microscopic examination revealed that the mucosa corresponding with the two ulcerated areas was completely necrotic and afforded direct access to the lumen of the cecum. The immediately adjacent areas were markedly inflamed and hemorrhagic. The rest of the mucosa was normal in appearance.

COMMENT

One of the most striking features noted in the study of the section from the buried stump was the combination of hemorrhagic infiltration and ulceration of the mucous membrane of the cecal wall distal to the insertion of the purse string suture. In spite of the fact that during the insertion of the suture no visible injury to the blood vessels and no visible hematoma was noted, the microscopic picture of hemorrhagic infiltration was a constant phenomenon. These changes could be readily seen with the naked eye in the mucous membrane of the inverted specimen. Microscopic examination shows clearly that these changes consist of hemorrhagic infiltration with ulceration of the mucosa. In contrast to this picture, examination of the unburied stump treated by simple ligation showed an absence of these features in every specimen examined. This experimental evidence bears out the clinical observation of Colp,¹⁴ who called attention to the danger of injury to the blood vessels during insertion of the inverting purse string suture.

Another interesting feature noted macroscopically was the frequent marked enlargement of the mesenteric lymph nodes in the experiments in which the stump was buried and the absence of this change when the stump was left unburied. This affords experimental confirmation of the clinical findings of Mayo, those of Riedel and those of de Martel, who observed and reported the presence of intense inflammation and changes in the cecal wall surrounding the buried stump. In several animals (rabbits 9, 11 and 14) pinhead-sized cecal abscesses were noted. In none of the experiments in which the stump was left unburied was any abscess formation observed. Adhesions were present in all of the experiments but were much more extensive in the experiments in which the stump was buried.

Distal to the ligature the stump proper showed massive necrosis in all instances. In the cases in which simple ligation was done there was

¹⁴ Colp R. *Ann Surg* 84:837, 1926.

an abrupt change at the site of the ligature. The tissue distal to the ligature showed massive necrosis. The tissue proximal to it was normal in appearance. In the cases in which the stump was buried, however, there were hemorrhagic infiltration and necrosis with ulceration of the mucous membrane in part of the cecal wall, between the purse string suture and the appendical ligature.

The stump in the cases in which it was left unburied was invariably covered by omentum or mesentery, and on microscopic examination newly formed connective tissue could be seen surrounding the entire stump distal to the ligature, completely separating it from all the surrounding viscera.

SUMMARY

In summarizing the salient features of the microscopic appearance of the specimen of buried appendical stump, the following observations may be noted:

The stump of the appendix is converted into massively necrotic substance. The cecal wall between the appendical ligature and the purse string suture in most parts appears perfectly normal but in some parts shows marked hemorrhagic infiltration separating the mucous membrane from the underlying tissue. In still other areas there is a complete loss of mucosa, with direct communication between the necrotic tissue of the stump and the lumen of the cecum. The picture is clearly that of a hemorrhagic infarct. In brief, the outstanding features are massive necrosis, hemorrhagic infiltration and ulceration of the mucous membrane, with direct communication between the lumen of the bowel and the necrotic contents of the buried stump.

In the stump treated by simple ligation the picture is different. There is no evidence of any hemorrhagic infarct. The stump itself undergoes necrosis and is completely separated from the rest of the cecum at the site of the ligature.

A definite zone of fibrous tissue forms around the stump, isolating it completely.

The process of healing in the buried stump is accompanied by marked adhesions between the stump and the surrounding tissue, marked lymphadenitis, occasional pericecal abscess formation, hemorrhagic infarction of the cecal wall between the appendical ligature and the purse string suture, ulceration of the mucous membrane in the area of infarction and massive necrosis of the stump.

In the ligated stump the healing process is accompanied by adhesions between the appendical stump and the surrounding tissue (less marked, however, than those found in the buried stump), necrosis of the stump

and formation of a definite zone of fibrous connective tissue around the stump. There is no hemorrhagic infarct, no lymphadenitis and no destruction of tissue proximal to the appendical ligature. These findings point clearly and definitely to the ordinary ligature (without inversion) method as the simplest, safest and most effective procedure in the treatment of the appendical stump.

After this paper had been completed, there was published by Ochsner and Lilly¹⁵ a method which it is claimed does away with all the dangers of a ligated buried stump and of postoperative hemorrhage. A purse string suture is passed in such a manner that the artery in the wall of the long axis of the stump is caught and the open stump of the appendix is inverted into the lumen of the cecum.

15 Ochsner, A., and Lilly, G. *Surgery* 2: 532, 1937.

TRANSPLANTED EPIPHYSIAL CARTILAGE

J DEWEY BISGARD, M D

OMAHA

In experimental animals long bones have been lengthened abnormally by increment from epiphysial cartilages transplanted to their shafts from neighboring bones. The grafts in these experiments were total massive segments, thick layers of adjacent bone from the epiphyses and diaphyses being included with the cartilage. Clinical application of the procedure has been precluded by the magnitude of the operation and the uncertainty of results.

In the experiments described here the possibility of lengthening bone by a less formidable procedure was investigated. All attempts, however, were unsuccessful.

EXPERIMENTS

In each of 8 goats approximately 1 month old two segments of the epiphysial cartilage plate with the adjacent layers of bone were removed from opposite sides of the femur and transplanted to the shaft of the tibia. The two segments of cartilage removed constituted less than half the plate, the central portion being left undisturbed. These segments were inserted between the two portions of the tibia, which had been divided transversely with resection of a complete segment of the shaft, equal in thickness to the graft to be interposed. The severed end of each portion was marked with a steel shot placed in a drill hole in the cortex. In all the animals the periosteum between the two portions was resected, and in 4 an additional cuff of periosteum 0.5 to 1 cm wide was removed. This was done in the hope of preventing the formation of a bridge of subperiosteal bone which would unite and lock the severed ends, thus preventing their distraction by bone laid down by the intervening growth cartilage. The legs were immobilized in plaster casts without padding. One animal lost its leg as a result of gangrene from circulatory interference. One had an infected wound with loss of the graft.

In the remaining 6 goats union was sufficiently firm in three weeks to permit removal of the casts. The animals were then observed for three months, and during this period there was considerable growth. During the first three weeks the distance between the shot was slightly diminished, but from that time on it remained unchanged. Thus, not only was there failure of the transplanted growth cartilage to contribute growth in length of the bone but a minute amount of shortening developed, presumably from absorption either of the cut ends or of the graft itself. One definite reason for this failure of the epiphysial cartilages to function is apparent in the roentgenograms taken three weeks after operation (figs 1 B and 2 B). In this short interval arching struts of newly formed bone

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had bridged the defect and united the two parts of the tibia around the periphery. This occurred despite the fact that the periosteum was resected and even after approximately 1 cm of the cut ends of the tibia had been denuded of periosteum. Although the presence of the cartilage definitely delayed central repair of the defect, it was gradually replaced by bone. At postmortem examination, three months after operation, no cartilage was found in 2 animals and only small scattered remnants in 4.

SUMMARY

After transplantation of segments of epiphyseal cartilage from the femur to the site of bisection of the shaft of the tibia, all growth in



Fig 1—Bisected tibia with a full thickness segment of epiphyseal cartilage interposed between the parts. The intervening periosteum was removed. The cut ends of the tibia were marked with steel shot placed in drill holes in the cortex. *A*, roentgenogram taken immediately after operation, *B*, roentgenogram taken three weeks after operation, *C*, roentgenogram taken three months after operation. Note the extent of repair in three weeks, the progressive replacement of transplanted epiphyseal cartilage by bone and the progressive lengthening of the bone. Note the slight shortening which took place during the first three weeks and that thereafter the shot remained equidistant. None of the growth in length, therefore, was acquired at the site of section from either the transplanted growth cartilage or the process of repair of the bisection. All growth took place at the epiphyseal ends of the shaft, the major portion at the proximal end.

the length of the tibia took place at the epiphysial ends. There was no interstitial growth. In no instance was length gained at the site of bisection. Soon after operation the distance between the shot used as markers became slightly less. Thus there was preliminary shortening from absorption either of bone at the severed ends of the tibia or of cartilage of the graft. Subsequently the shot remained equidistant.

Slight separation of the parts of the tibia and resection of the intervening periosteum did not prevent union, nor did absence of periosteum from the severed ends. It must be remembered, however, that the animals used (goats) were very young and, like all newborn animals, had tremendous propensity for repair and growth.

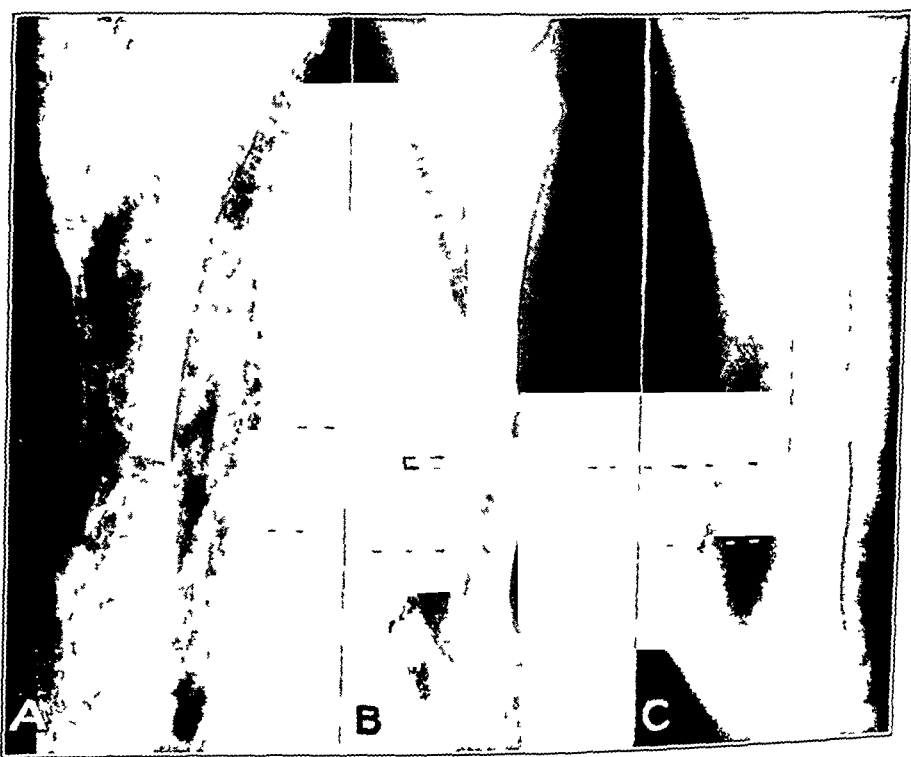


Fig 2—Bisected tibia treated like that in figure 1 except that the periosteum was resected from the ends of the parts for a distance of approximately 1 cm. The roentgenograms were taken (A) one day, (B) three weeks and (C) three months after operation. In the absence of periosteum, union by bridging struts of new bone took place rapidly but less profusely than in the animal represented in figure 1. Similarly, the shot remained equidistant after a slight preliminary shortening of the intervening distance during the first three weeks. Thus all growth in length was acquired from the epiphysial cartilages at the ends of the bone.

Full thickness segments of the epiphysial cartilage interposed in the tibial shafts failed to contribute length. Literally, these grafts were imprisoned and unable to give increment had this function otherwise been preserved.

INTUSSUSCEPTION DUE TO HEMANGIOMA OF THE JEJUNUM

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There has always been considerable interest in benign tumors of the small intestine because of their extraordinary infrequency and the serious or even fatal complications which may be associated with them. Kassemeyer¹ in 1912 was able to collect 78 cases of benign tumor of the small bowel from a total of 284 cases of benign tumor of the gastrointestinal tract as a whole. King² in 1917 reviewed the literature and reported 50 cases of benign tumor of the small intestine. Raiford³ in 1932 collected 50 cases in a study of 11,500 autopsies and 45,000 surgical specimens at the Johns Hopkins Hospital. Rankin and Newell⁴ in 1933 were able to find only 35 cases in the records of the Mayo Clinic. The cause of such tumors and the reasons for their infrequency have never been satisfactorily explained, although Raiford stated the belief that the unsusceptibility of the small intestine to tumor growth is associated with the embryologic, anatomic and physiologic peculiarities of this region. No age period is exempt, although benign tumors tend to occur more frequently in the earlier decades, while malignant tumors are characteristic of the later years.

In summarizing the records of the Royal Victoria Hospital and the Pathological Institute it was found that there were 6 benign tumors of the small intestine among 50,775 surgical specimens examined between the years 1915 and 1939. Eighteen cases were observed in 7,340 autopsies performed from Jan. 1, 1915 to May 1, 1939. Histologic examination of these 24 tumors resulted in the following diagnoses: lipoma, 6; fibroma, 4; adenoma, 3; adenomatous papilloma, 3; hemangioma, 3; carcinoid, 2; fibroadenoma, 1; fibromyxoma, 1; and

From the Department of Pathology, Pathological Institute, McGill University, and the Royal Victoria Hospital.

1 Kassemeyer, E. Tumorinvagination des Darms, *Deutsche Ztschr. f. Chir.* **118** 205, 1912.

2 King, E. L. Benign Tumors of the Intestine with Special Reference to Fibroma, *Surg., Gynec. & Obst.* **25** 54, 1917.

3 Raiford, T. S. Tumors of the Small Intestine. *Arch. Surg.* **25** 122 (July), 321 (Aug.) 1932.

4 Rankin, F. W., and Newell, C. E. Benign Tumors of the Small Intestine, *Surg., Gynec. & Obst.* **57** 501, 1933.

lymphoma, 1 Secondary growths, cysts, embryonic rests and the like were excluded Three glandular polyps (non-neoplastic) were omitted The 24 tumors were located in the small bowel as follows duodenum, 6, jejunum, 6, and ileum, 12 Intussusception was reported in 7 cases, or 29 per cent

It was observed, however, that the incidence of benign tumors of the small intestine in no way indicated the frequency with which these tumors were encountered in the gastrointestinal tract as a whole (from cardia to anus) During the same period (1915 to 1939), a total of 274 benign tumors of the entire gastrointestinal tract were collected Of these tumors, 174 were obtained from the surgical specimens and 100 from the postmortem material The tumors were located in the digestive tract as follows stomach, 43, small bowel, 24, cecum, 13, colon, 31, sigmoid flexure of colon, 19, rectum, 114, and anus, 30 Again, questionable or secondary tumors, embryonic rests and growths showing probable early malignant changes were not included The incidence of benign tumors of the small intestine was, therefore, 87 per cent of all such neoplasms in the tract, while that of hemangiomas in the same region was 109 per cent

Of the benign tumors of the small bowel reported, those of vascular origin are among the most rare It is interesting to observe that Gascoyen⁵ is given credit for reporting the first case of hemangioma of the bowel In the series of cases noted, King² found, 1, Raiford,³ 3, and Rankin and Newell,⁴ 2, and I found 3, 2 of which are reported here Brown⁶ in 1924 reviewed the literature and collected 20 cases of vascular tumor of the intestine He found no relation between the sex and age of the patient and the number of tumors present McClure and Ellis⁷ in 1930 collected 25 cases, many of which were listed in Brown's group, and found the ages of the patients to range from 2 months to 79 years Recently, Ackerman⁸ has added 2 cases of cavernous hemangioma of the small intestine and 1 case in which tumors occurred in both the small and the large intestine In general, the hemangiomas were of two types the capillary type, with an abundant overgrowth of small blood vessels which may appear immature and angioblastic or mature with smooth muscle and fibrous tissue and the

5 Gascoyen Case of Naevus Involving the Parotid Gland, and Causing Death from Suffocation Naevi of the Viscera, *Tr Path Soc London* **11** 267, 1860

6 Brown, A J Vascular Tumors of the Intestine, *Surg, Gynec. & Obst* **39** 191, 1924

7 McClure R D, and Ellis, S W Hemangiomata of the Intestinal Tract *Am J Surg* **10** 241, 1930

8 Ackerman, L V Cavernous Hemangiomata of the Small and Large Bowel *Am J Cancer* **30** 753, 1937

cavernous type, with large, dilated blood-filled cavities, usually having a single endothelial cell lining with or without a smooth muscle wall

These tumors in the intestine have been further classified by Brown into the following groups: 1 Multiple tumors of vascular arcades forming nodules in the submucosa and associated with the arteries or veins. They form vascular nevi or cavernous hemangiomas. 2 Submucosal tumors which grow toward the lumen of the intestine and may become ulcerated by pressure or trauma. 3 Submucosal tumors which may become polypoid in structure and grow to a size sufficient to obstruct the lumen or to bring about an intussusception. 4 Diffuse ringlike tumors which begin in the submucosa and involve the muscularis so that the lumen is constricted and an acute or chronic obstruction results. Malignant degeneration is occasionally reported (Winternitz and Boggs⁹).

The signs and symptoms of these vascular tumors are usually those of intestinal obstruction, hemorrhage or acute inflammation, although in about half the reported cases they were asymptomatic and were seen incidentally at operation or necropsy. The obstruction was attributable to encroachment on the lumen, to volvulus or to intussusception. Of these, intussusception was the least frequent.

Nicoll¹⁰ in 1899 reported the first cases of intussusception at the site of a cavernous hemangioma. A survey of the literature over the last twenty years revealed only 2 other reported cases. McClure and Ellis observed 1 at operation in 1930, Weber¹¹ reported the last in 1936. Even at operation, however, one may fail to identify a vascular tumor as the cause of an intussusception, owing to the edema, infiltration and gangrene of the involved bowel or because of the gravity of the situation and the necessity for the surgeon to finish the abdominal procedure as quickly as possible. Although Raiford found intussusception to occur with 23 per cent of her series of benign tumors of the small bowel, it was not present in any of the patients with hemangioma. Rankin and Newell, with a general incidence of 17 per cent, found none in cases in which the tumors were vascular. Willis¹² collected 19 cases of intussusception due to adenoma from 7,492 autopsies at the Boston City

9 Winternitz M C and Boggs T R. A Unique Coincidence of Multiple Subcutaneous Hemangio-Endothelioma, Multiple Lymphangio-Endothelioma of the Intestinal Tract and Multiple Polypi of the Stomach Undergoing Malignant Changes Associated with Generalized Vascular Sclerosis and Cirrhosis of the Liver, *Bull Johns Hopkins Hosp* **21** 203 1910

10 Nicoll, J H. On the Removal of a Naevoid Tumor of the Intestine. *Brit M J* **1** 843 1899

11 Weber, H. Invaginatio ileocecalis, bedingt durch ein Haemangioma simplex. *Centralbl f allg Path u path Anat* **66** 33 1936

12 Willis A W. Intussusception Resulting from Benign Tumors of the Intestine. *Surg Gynec & Obst* **30** 603 1921

Hospital and the Massachusetts General Hospital, but in no instance was the condition due to hemangioma. Perrin and Lindsey¹³ reviewed 400 cases of intussusception, Roan¹⁴ 100, King² 18 and Winthrop¹⁵ 18, but they cited no case of intussusception due to a vascular tumor. Biggs¹⁶ discussed the problems of intussusception but failed to mention vascular tumors as an etiologic factor.

Recently I have had occasion to perform autopsy in 2 cases of intussusception due to hemangioma of the jejunum, and these are the only 2 cases on record at this institution of this type of intestinal obstruction caused by a benign vascular tumor of the small intestine. In 1 of them the condition was further complicated by hemangiomatosis involving the skin, stomach, kidney and adrenal gland. Because of this and the rarity of the condition, it was considered worth while to report these cases. In the only other case of hemangioma of the small bowel (jejunum) in the records of this institution the growth was found incidentally at autopsy. The tumor had caused no symptoms or complications, and hence the case will not be reported here in detail.

The diagnosis of vascular tumor of the bowel usually is obscure and is not made preoperatively, but the presence of such a tumor may be suspected on the basis of abdominal symptoms and the history or evidence of hemangiomas in other areas. According to Ackerman, a correct diagnosis should usually be made in "the presence of visible hemangiomata, obscure hemorrhage, and signs of acute or chronic obstruction, together with x-ray findings" suggestive of this condition (Judd and Rankin¹⁷).

REPORT OF CASES

CASE 1—A S, a 67 year old white woman, was admitted to the Royal Victoria Hospital on July 26, 1938, complaining of sudden onset of pain in the right lower quadrant of the abdomen, nausea and vomiting for two days and chronic constipation. There was no history of loss of weight, weakness or previous digestive distress. The family and functional histories were noncontributory. Physical examination showed the temperature to be 99.3 F, the pulse rate was 96, and the respiratory rate, 20. The patient was emaciated, edentulous and dehydrated. There were no visible hemangiomas of the skin or mucous membranes. The lungs were clear. The heart was not enlarged, and the blood pressure was 128 systolic and 80 diastolic, but there were gallop rhythm and extrasystoles. There were splinting

13 Perrin, W S, and Lindsey, E C. Intussusception. A Monograph Based on Four Hundred Cases, *Brit J Surg* 9 46, 1921.

14 Roan, O. Intussusception Due to Benign Tumors of the Small Bowel. *Texas State J Med* 27 782, 1932.

15 Winthrop, G J. Chronic Enteric Intussusception Due to Intestinal Tumors. *J A M A* 64 1303 (April 17) 1915.

16 Biggs, M H. Intussusception of the Ileum in Adults Due to Benign Tumors, *Surg, Gynec & Obst* 33 490, 1921.

17 Judd, E S, and Rankin, F W. Hemangiomas of the Gastrointestinal Tract, *Ann Surg* 76 28, 1922.

of the abdomen over the right side, tenderness beneath the right costal margin, enlargement of the liver and a palpable mass high in the right lower quadrant of the abdomen. The other systems were normal. The laboratory findings were as follows: leukocytes, 12,000 per cubic millimeter, urine, normal, stool, acholic and free of blood, value for nonprotein nitrogen, 23.5 mg per hundred cubic centimeters, carbon dioxide-combining power, 49.3 mg per hundred cubic centimeters, value for blood sugar (with the patient fasting), 75 mg per hundred cubic centimeters. A diagnosis of acute appendicitis with abscess formation was made.

Course—At operation, on July 27, an acutely inflamed, gangrenous ruptured gallbladder was found, with diffuse bile peritonitis. Cholecystotomy was done. The patient progressed fairly well, but on September 25 further exploration was necessary because of complete obstruction of the common bile duct. Convalescence was uneventful until September 29, when she suddenly went into shock and died.

Postmortem Examination—There were no cutaneous lesions other than the healing McBurney incision and the 20 cm recently closed right paramedian incision. There was evidence of diffuse peritonitis. The gallbladder was small, thick, black, lusterless and bound down by adhesions. The bile ducts and the ampulla of Vater were patent. There was no tumor in this region. The duodenum was filled with blood, as was the upper part of the jejunum to a point 40 cm from Treitz's ligament. Here there was an intussusception measuring 20 cm in length. At the distal end a round mass could be felt within the lumen, which on exposure was found to be a rounded polypoid tumor 3 cm in diameter, with a broad base (fig 1). The walls of the jejunum proximal to the intussusception and the duodenum were hemorrhagic.

Microscopic sections showed the tumor of the jejunum to consist of vascular channels of variable size, ranging from small capillary-like structures to large cavernous and cystic spaces. In some places the lining endothelium was composed of a single layer, in others it was piled up. The connective tissue stroma varied considerably in amount. The tumor evidently had arisen from the submucosal vascular plexus (fig 2). The diagnosis was polypoid hemangioma. Sections of the jejunum revealed generalized congestion but no degeneration or necrosis of the tissue. Other sections showed exudative, necrotic cholecystitis, fibrosis of the ampulla of Vater, productive pleurisy, bronchopneumonia and adenoma of the thyroid.

Comment—The diagnosis of intussusception due to hemangioma of the jejunum was made only at autopsy, as all the evidence indicates that the intussusception occurred shortly before death. It is well recognized (Rankin and Newell,⁴ Biggs¹⁶) that the occasional intussusception encountered in the adult is most frequently caused by a neoplastic growth in the intestinal tract, in contradistinction to the spontaneous intussusception frequently encountered in children. In my opinion, the symptoms and signs of shock as noted in the history are explained by the occurrence of the intussusception and by the massive hemorrhage into the small bowel above the obstruction. The hemorrhage may have occurred from the vascular polyp, from the intestinal mucosa or from both; it was not possible to demonstrate conclusively which. It is interesting to observe that no other hemangiomas were found in the patient.

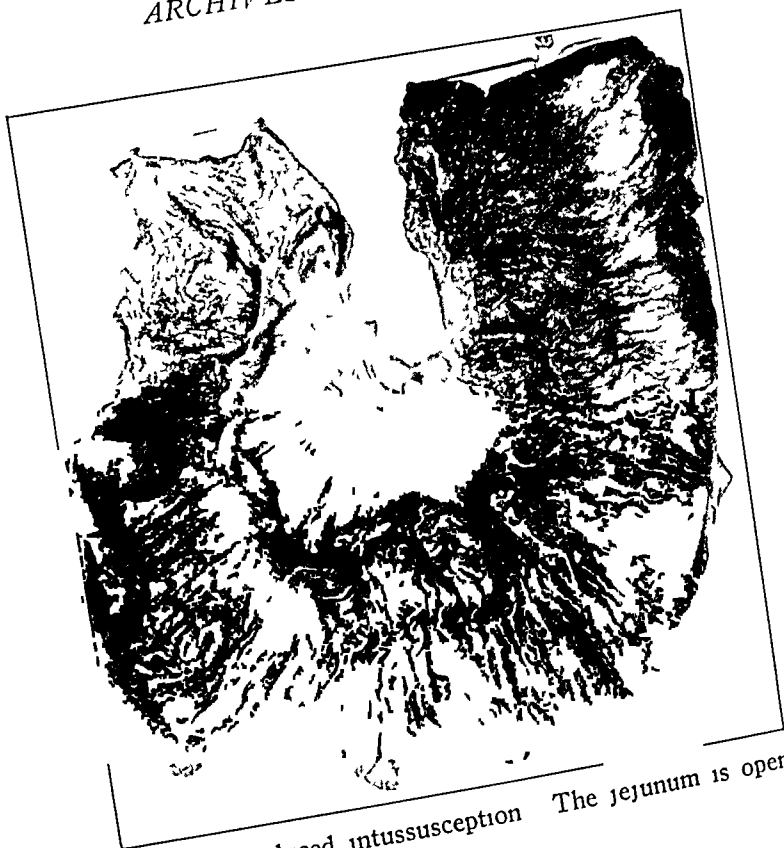


Fig 1 (case 1) —Reduced intussusception The jejunum is opened to demonstrate the polypoid hemangioma

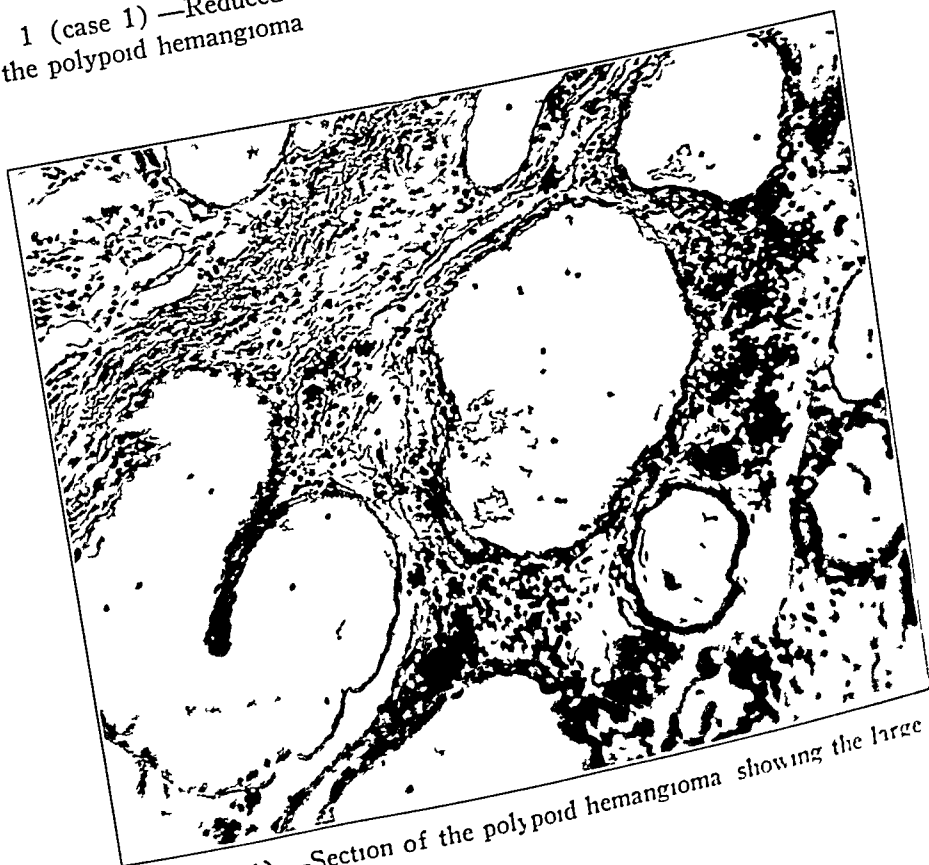


Fig 2 (case 1) —Section of the polypoid hemangioma showing the large blood filled cavities, $\times 200$

CASE 2—R M, an 8 year old white boy, was admitted to the Royal Victoria Hospital on April 12, 1939, complaining of pallor and anorexia for three weeks and of sudden onset of crampy abdominal pain and vomiting twelve hours before subsequent to a mild purge. This patient was first admitted to the hospital on Oct. 5, 1930, when only 3 days old, at which time the lower lip was found to be replaced by a large blue hemangioma measuring 2.5 by 1.5 by 1 cm. There were 19 other vascular tumors scattered over the scalp, body and extremities, varying from the size of a pinpoint to 1 cm in diameter. The child had been otherwise normal at birth, and the family history was noncontributory. The hemangioma of the lip was excised and the diagnosis confirmed by pathologic study of the surgical specimen. The tumor recurred, however, when the patient was 3 months old, and since then there had been fourteen other admissions to the hospital, for excision or coagulation of the tumor or for plastic repair of the lip. These operations had been unsuccessful because of persistent recurrence of the tumor. Melena was never noted, although the records show rather constant hypochromic anemia throughout the eight years.

Physical examination on April 12 revealed a temperature of 99 F, a pulse rate of 136 and a respiratory rate of 30. The patient was extremely thin, pale, undernourished, restless and drowsy. There were numerous scars on the body and multiple hemangiomas over the trunk and extremities and beneath the nails. The lower lip was markedly deformed and largely replaced by scar tissue. No tumor was seen at this time. There was a soft, blowing, mitral systolic murmur and the blood pressure was 110 systolic and 80 diastolic. A mass was visible in the middle of the lower part of the abdomen, rising to the level of the umbilicus. It was about 8 cm in diameter, doughy, irregular, dull to percussion, nonfluctuant and not movable on respiration. The mass itself was tender, but there was no generalized abdominal tenderness or rigidity. Peristalsis was not noted. Laboratory findings were as follows: white blood cell count, 19,000 per cubic millimeter, red blood cell count, 2,900,000 per cubic millimeter, hemoglobin, 35 per cent, stools, free of blood, urine normal, nonprotein nitrogen content of blood, 21.4 mg per hundred cubic centimeters, carbon dioxide-combining power, 42.5 mg per hundred cubic centimeters, chloride content of the blood 323 mg, and sugar content (with the patient fasting), 135 mg per hundred cubic centimeters. Roentgenograms taken with and without contrasting mediums showed what appeared to be a soft tissue mass lying over the fourth or fifth lumbar vertebra on the right, with a slight amount of gas in the small bowel to the left but no evidence of intussusception. A tentative diagnosis of intestinal hemorrhage with obstruction due to volvulus, internal hernia or intussusception was made. Operation was delayed on the strength of the roentgenograms and because of the poor condition of the patient.

Course—The following day the patient seemed to be improved although the mass was still present. On April 14, however, he became worse, the pain and the pulse rate increased and the temperature rose to 101 F. A roentgenogram taken at this time showed marked distention of the small bowel on the right and suggested intestinal obstruction. Immediate exploratory operation was done with the patient under nitrogen monoxide-oxygen-ether anesthesia. An intussusception 30 cm long was encountered at a distance of about 40 cm from the ligament of Treitz. This was reduced with difficulty. Near the head of the intussusception a rather large tumor mass was found in the wall of the jejunum, which to external examination was thick and protruded into the lumen but was not polypoid. A small weakened area near the mesentery at one point was closed over with sutures. The bowel was believed to be viable. The abdomen was closed and drained with-

out further operative procedure because of the poor condition of the patient. Postoperatively the temperature rose to 106.3 F and the pulse rate to 170, the abdomen became distended, and there was vomiting and a typical hippocratic facies. Continuous nasal suction and supportive treatment were given but produced no relief, and the boy died April 16, 1939.

Postmortem Examination—There was marked deformity of the mouth, and the skin appeared thin and blue, but no tumor of the lip could be identified. There were innumerable hemangiomas on the body, as has been mentioned. In the upper part of the abdomen there was localized peritonitis. At a distance of 70 cm from the ligament of Treitz the jejunum became greatly discolored and covered by exudate for about the same distance. About one third of the way from the beginning of this affected bowel there was a tumor-like mass 15 by 15 cm in



Fig 3 (case 2)—Portion of the jejunum containing the hemangioma, which has been exposed by cross section

the wall. This seemed to be about 0.5 cm in thickness (fig 3) and resembled a hemangioma. Nearby, close to the mesentery, were two small perforations from which intestinal contents were pouring. Small hemangiomas were observed in the stomach, the left kidney and the left adrenal gland.

Microscopic sections showed the tumor mass to consist of cavernous communicating channels lined by rather dense fibrous tissue and devoid of fresh blood. A single endothelial cell lining was seen, but finer structures had been destroyed by the associated degenerative and necrotic enteritis in this section of the jejunum. A diagnosis of hemangioma with productive changes was made. Sections of the tumors of the stomach (fig 4), skin, adrenal gland and kidney gave an essentially similar picture. These showed numerous distended large and small cavernous channels, all lined by a more or less single layer of endothelial cells. Special stains failed to show elastic tissue fibers but did show an occasional structure

smooth muscle. Other sections showed confluent bronchopneumonia, catarrhal lymphadenitis and hyperplasia of the bone marrow. There was no intussusception at the time of autopsy.

Comment—This case clearly indicates the serious and fatal complications which may arise from a benign hemangioma of the jejunum which has resulted in intussusception. The case illustrates most of the points outlined by Ackerman⁸ for the diagnosis of intestinal obstruction due to vascular tumors. It is unfortunate that the intussusception had

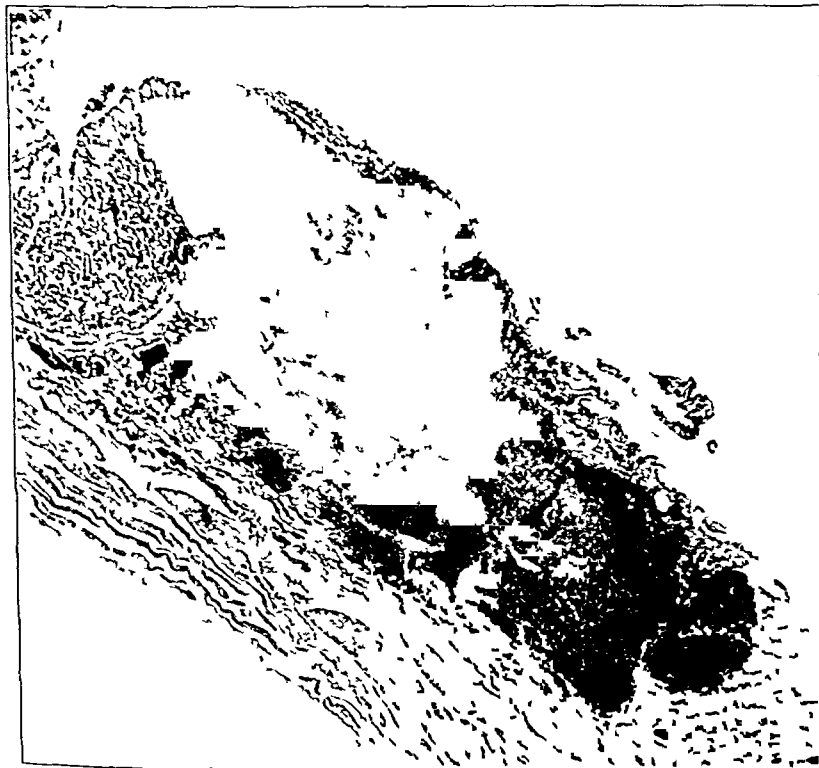


Fig 4 (case 2) —Section of the submucosal hemangioma of the stomach, which is pushing outward into the cavity and has thinned the overlying mucosa, $\times 10$

continued until the bowel was gangrenous and perforation with fatal peritonitis had occurred. The multiplicity of the tumors and their marked tendency to recur, however, make it extremely unlikely that the prognosis could have been anything but poor.

It is interesting to observe that these 2 cases represent distinctly different age periods, one the first and the other the sixth decade. Histologically, the vascular tumors in both were primarily of the cavernous type. In the only other case of hemangioma of the small

bowel found in the records of the Royal Victoria Hospital there were innumerable small submucosal cavernous hemangiomas in the jejunum of a man aged 64 who died of hypertensive heart disease

GENERAL COMMENT

Two cases of hemangioma of the jejunum complicated by intussusception are added to the meager literature on the subject. The difficulties of making a clinical diagnosis in such cases have been well demonstrated. The cases reported constitute the only instances of this combination of conditions in the records of the Royal Victoria Hospital and the Pathological Institute between the years 1915 and 1939. One other case of hemangioma of the small bowel, without intussusception, has been observed. These 3 cases comprise 1.09 per cent of all cases of benign tumor of the gastrointestinal tract from the cardia to the anus and 12.5 per cent of those of benign tumor of the small bowel.

It is not the purpose of this report to enter into a discussion as to whether cavernous hemangiomas like those occurring in my 2 cases are to be considered true tumors or simple vascular malformations. They are generally classified as neoplasms. The progressive growth and persistent recurrence which occurred in other parts of the body in the second case certainly indicate a neoplastic process. Should the reader be interested in this subject, reference may be made to the studies of Sabin¹⁸ and of Geschickter and Keasly¹⁹.

SUMMARY AND CONCLUSIONS

Hemangiomas of the small bowel are rare, and complications due to intussusception are very infrequent. This complication is serious and often fatal and may be suspected whenever symptoms of intestinal obstruction and hemorrhage occur with a history or evidence of hemangiomas elsewhere in the body. Two cases of this comparatively rare condition are reported.

18 Sabin, F. R. Preliminary Note on the Differentiation of Angioblasts and the Method by Which They Produce Blood Vessels, Blood Plasma and Red Blood Cells as Seen in the Living Chick, *Anat. Rec.* **13** 195, 1917.

19 Geschickter, C., and Keasly, L. E. Tumors of Blood Vessels, *Am. J. Cancer* **23** 568, 1935.

PRODUCTION OF EXPERIMENTAL TUMORS OF THE BRAIN WITH THE SHOPE RABBIT PAPILLOMA II

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AND

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The gross characteristics of extradural and subdural growths produced by implantation of virus-induced cutaneous rabbit papilloma¹ and the reaction of the brain to such experimental tumors have been described briefly². It was noted in a small series of implantations that the intracranial growths were essentially similar to those observed following implantation in other tissues of the host. The proliferating epithelium of the individual growths did not invade the adjacent nerve tissue, and the growths thus presented the picture of slowly expanding intracranial tumors. Histologic study showed that there was no glial reaction when implantation was extradural and a layer of meninges was interposed between the tumor and the brain. When, on the other hand, the tumor was implanted subdurally, thus coming into more direct contact with the parenchyma of the brain, there was always proliferation of astrocytes with formation of numerous fibers, which were attached to the tumor cells.

In the preliminary studies, difficulty was encountered in obtaining growths by implantation within the brain substance. Improvements in technic have made possible the production of such growths in a high percentage of animals. In the present work the behavior of papilloma transplanted into the brain tissue has been studied. Further observations of extradural and subdural implants have been made in a larger series of animals. The results of these experiments and those of a study of the general reaction of the host to slowly expanding intracranial tumors are described here.

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¹ Shope, R. E. Infectious Papillomatosis of Rabbits, *J. Exper. Med.* **58**: 607-624, 1933.

² Woodhall, B., Graves, R. W., and Beard, J. W. Experimental Production of Tumors of the Brain with the Shope Rabbit Papilloma, *Arch. Surg.* **38**: 457 (March) 1939.

METHOD

The preparation of the virus, the production and histologic character of the cutaneous papilloma and the technic of extradural and subdural implantation have been described in detail.² Early attempts to implant the papilloma intracerebrally by injecting fragments through a short 18 gage needle were unsuccessful, but consistent implantation was accomplished in the following manner. Through a sagittal incision 4 mm to the left of the midline of the skull a perforator opening was made in the desired longitudinal plane (in the majority of instances on the left side over area 17 as demarcated for the rabbit brain), large enough to accommodate a short, flanged ventricular needle. After preliminary incision of the dura the ventricular needle was passed into the brain tissue for a distance of 8 mm from the surface of the skull. Ventricular fluid was frequently encountered, puncture deeper than the lateral ventricle resulted fatally in 1 instance from hemorrhage into the basal ganglions. Hashed papilloma tissue was readily pushed through the relatively large lumen of the ventricular needle. The needle was 25 mm in diameter, and the necessary aperture in the skull was not large enough to destroy the conception of the skull as a rigid container.

Further studies were made by extradural and subdural implantation methods with a view toward securing tumors in these sites larger than those previously described. The rabbits were killed at various intervals after implantation of the tumor tissue and the cranial vessels were washed out with 0.9 per cent sodium chloride solution through the carotid arteries prior to fixation in alcohol or in formaldehyde-ammonium bromide solution. Thirty animals were used in the combined study, of these, 6 died during or shortly after the operative procedure, 5 were killed at appropriate intervals and were found to be without tumors, and 19 showed intracranial growths.

GENERAL CHARACTER OF GROWTHS RESULTING FROM
INTRACEREBRAL TRANSPLANTATION

The papilloma was readily transplanted intracerebrally by the simple technic described. This procedure was carried out in 8 rabbits, in 5 of these intracerebral tumors were produced, and 3 animals died during implantation or within one week. One of the last-mentioned group died of hemorrhage as the result of faulty technic, and the other 2 showed satisfactory implantations but succumbed to dysentery. The general reactions of the hosts in which the 5 successful implantations were made may best be described by presenting in detail a typical protocol.

Rabbit 206, thirty-nine days after intracerebral implantation of the growth on the left side, exhibited definite signs of increasing intracranial pressure. Both forelegs were weak, the right more than the left. Muscle tone was increased in the right foreleg. Both pupils were small, the left being larger than the right. Both optic disks appeared constricted or of decreased diameter as compared with the normal and the margins of both were elevated. Ventricular fluid had not been obtained at the time of implantation. When the animal was killed and the skull cut away, no tumor was apparent over the convexity of the brain, though the convolutions were flattened over the regions corresponding to areas 5 and 7. A cross section of the brain disclosed a subcortical tumor measuring 12.5 by 15 mm. The growth had displaced the basal ganglions to the right and had caused the development of a lateral hydrocephalus involving the ipsilateral frontal horn.

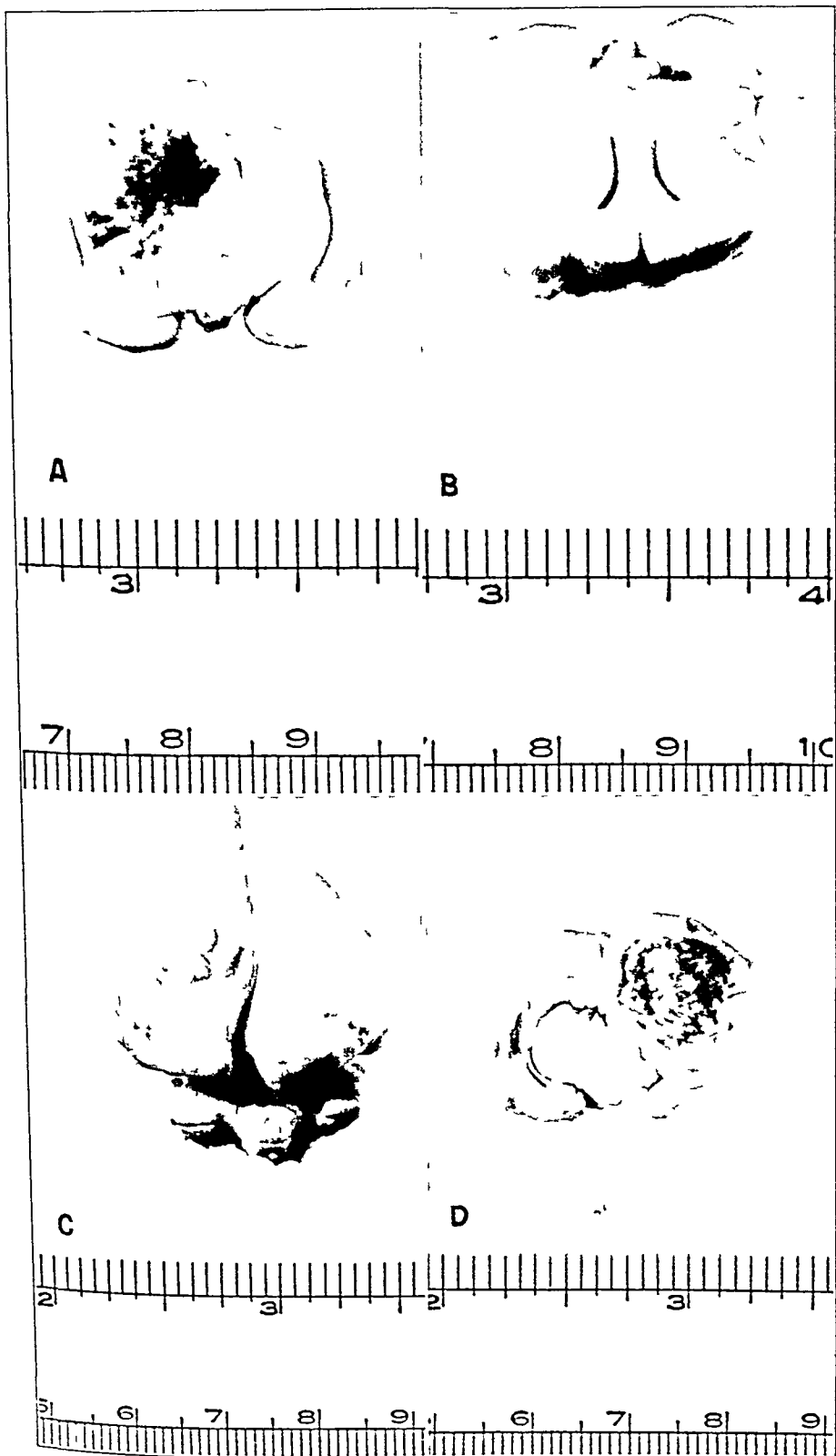


Fig 1—A cross section of an intracerebral tumor (rabbit DR 206) $\times 1\frac{1}{2}$
 B, hydrocephalus resulting from a left-sided intracerebral tumor in areas 5 and 7
 (rabbit DR 206) $\times 1\frac{1}{2}$ C external configuration of a hemisphere with an
 intracerebral tumor implanted in the left side (rabbit DR 315) The animal, not
 described in the text showed paresis of the right extremities and anisocoria the
 left pupil being larger than the right The illustration is natural size D, cross
 section of an intracerebral tumor (rabbit DR 315) natural size

All growths, including the one just described, were situated in the left hemisphere, beneath the original bony defect, and had expanded in a concentric fashion from this median point. The tumor masses were firmly embedded in the nerve tissue and when cut across could be dislodged only by forceful manipulation. There was no gross evidence of invasion of the nerve tissue, but the growths were definitely adherent to the adjacent brain substance. In shape and general appearance the intracerebral tumors were similar to the growths described in our earlier publication². They were elastic and roughly spherical, and the presenting surface of each was irregular and creamy white. On section the external layer showed as a kind of whitish succulent tissue about a dense, situated creamy or grayish black necrotic mass.

Three of the five intracerebral growths were from 11 to 15 mm in diameter, the remaining two were 3 mm and 5 mm, respectively. The period of maximum growth compatible with the well-being of the experimental animal appeared in this small series to be from thirty-five to fifty-two days after implantation. The 3 mm and the 5 mm growth were obtained, one fifteen days and the other, thirty-nine days, after, in neither instance had the animal displayed unusual neurologic manifestations. The 3 animals with large growths showed definite impairment of consciousness, progressing to deep coma in 1 instance. Two of the 3 animals showed a motor deficit with spasticity contralateral to the tumor, anisocoria with the dilated pupil on the side on which the lesion was present and a questionable abnormality of the optic disks. The third animal was not examined neurologically. All 3 showed hydrocephalus on section of the brain.

GENERAL CHARACTER OF MORE ADVANCED GROWTHS RESULTING FROM SUBDURAL IMPLANTATION

Fragments of papilloma were implanted subdurally in 10 animals in an effort to produce large intracranial growths to further the study of the effects of increasing intracranial pressure on brain tissue. Each implantation was successful in producing the desired growth. In 3 animals, rabbits DR 409, DR 320 and DR 114, killed, respectively fifteen, twenty-one and forty-two days after implantation, small, entirely subdural growths were found, they were similar to those previously described, measuring in each instance 4 by 4 mm. The growths were fixed in appropriate solutions for histologic study.

In the remaining 7 animals the tumors were of two distinct types. Two animals showed large subdural tumors with an extension into the cerebral tissue that represented in each case a true intracerebral growth. In 5 animals the subdural-intracerebral growth was associated with an extradural tumor, the connection between the two being marked by

thin strand of tumor cells extending through the original dural incision. In 3 of the 5 there was also an extracranial extension of the extradural growth through the tiny perforator opening in the skull. The adjacent bone was thickened and vascular. The effects of the subdural-intracerebral tumors may be described to advantage by presenting the protocol of a typical experiment.

Rabbit 168 was killed forty days after subdural implantation of tumor on the left side. At this time the animal was found lying on its right side. On examination there was no localized paresis or change in muscle tone, but the animal did not make use of its right extremities as fully as of its left. No definite change could be made out in either fundus. The left pupil was larger than the right.

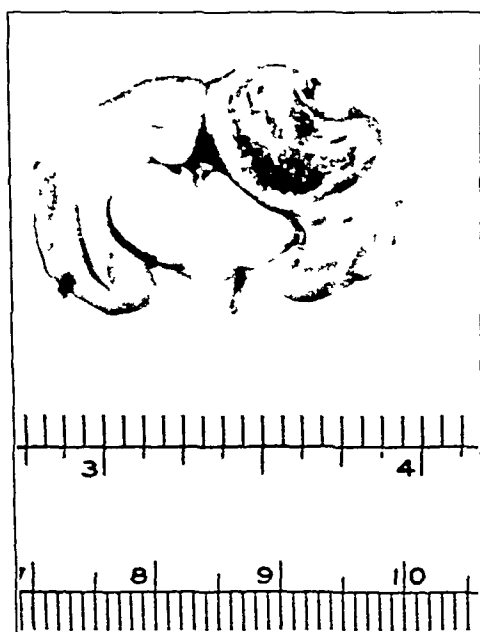


Fig 2—Cross section of subdural-intracerebral tumor (rabbit DR 168) $\times 1\frac{1}{2}$

There was a coarse irregular nystagmus affecting the left eye, with the quick component toward the assumed center of fixation. When the scalp was reflected an extracranial tumor 3 by 3 mm was noted protruding through the perforator opening. When the skull was removed, the intracranial tumor was apparent superficially as an oval mass 6 by 8 mm lying in the left temporo-occipital region and extending caudally beyond the occipital pole for a distance of 3 mm. On cross section the subdural growth was found to extend as a large intracerebral growth 11.5 by 9.5 mm which depressed the basal ganglions and expanded subcortically from area 17 into area 18. Both frontal horns of the ventricular system were dilated (fig 2).

The remaining 5 animals had extradural-subdural growths, two of which are described in the following protocols.

Rabbit DR 122 was killed fifty-five days after subdural implantation of tumor on the right side. While being handled the animal had a generalized convulsion which seemingly involved the extremities of the left side more than those of the right. The hyperactive clonic movements persisted for twenty or more seconds, and the reaction was repeated on any passive movement of the extremities during a short period of observation. There was no anisocoria. A more detailed neurologic study was not done. When the scalp was reflected, a flat extracranial tumor 3 mm in diameter was protruding through the perforator opening. On removal of the skull plate an extradural tumor was noted, measuring 9 by 8 mm and projecting 3 mm above the surrounding cortex. It was rostral to area 17 and

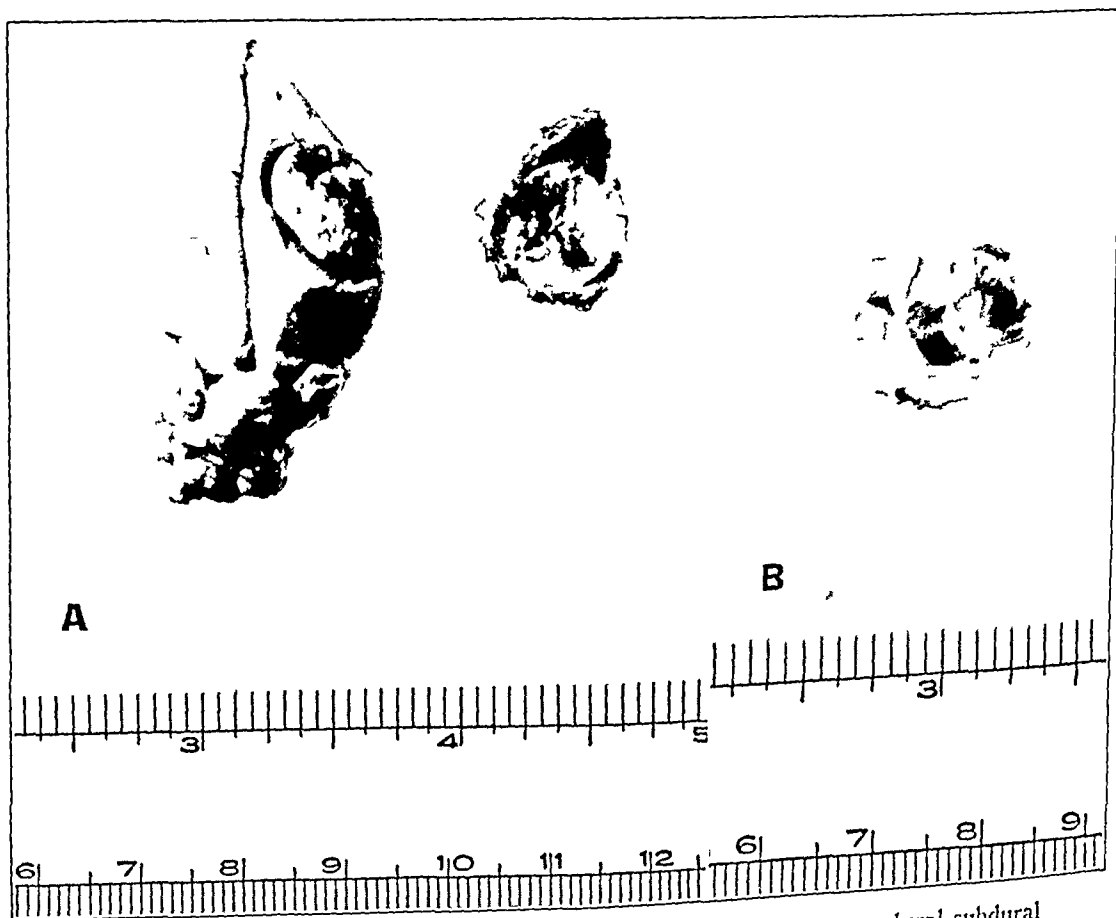


Fig 3—*A*, external configuration of a hemisphere with an extradural-subdural tumor in situ (rabbit DR 122), natural size. *B*, cross section of a rostrally placed extradural-subdural tumor (rabbit DR 122) with associated contralateral hydrocephalus of the frontal horn, natural size.

was the most anteriorly placed tumor of the series. Two thirds of the tumor mass was found on section to be situated extradurally and the remainder subdurally. The entire mass was 10 by 11 mm in cross section. Marked hydrocephalus had developed in the contralateral ventricle and in the ipsilateral posterior horn (FIG 3).

Rabbit DR 201 was found lying in its cage in a position of opisthotonus, eighty-six days after a midline cerebellar implantation of tumor. Its head was held in constant retraction, and all four extremities were in extensor spasm, with a constant fine tremor of the forelegs. The animal rapidly resumed this position

on passive movement by the observer. There was no anisocoria. Both disks appeared normal. There was a persistent horizontal nystagmus with the quick component to the left in each eye, that is, forward in the right eye and backward in the left. When the scalp was reflected, a large extracranial tumor presented, measuring 14 by 11 by 8.5 mm. When the bone case was removed an extradural tumor was seen, measuring 16 by 16 mm. When the extradural tumor was lifted from its bed a subdural extension was noted, measuring 10 by 7 by 6 mm, making the entire tumor 13.5 mm in depth. This huge tumor compressed both occipital poles, particularly the left, and formed a deep indentation in the anterior third of the cerebellar vermis. The left half of the pons was markedly compressed, and the defect on the right side was perhaps one third as deep. The

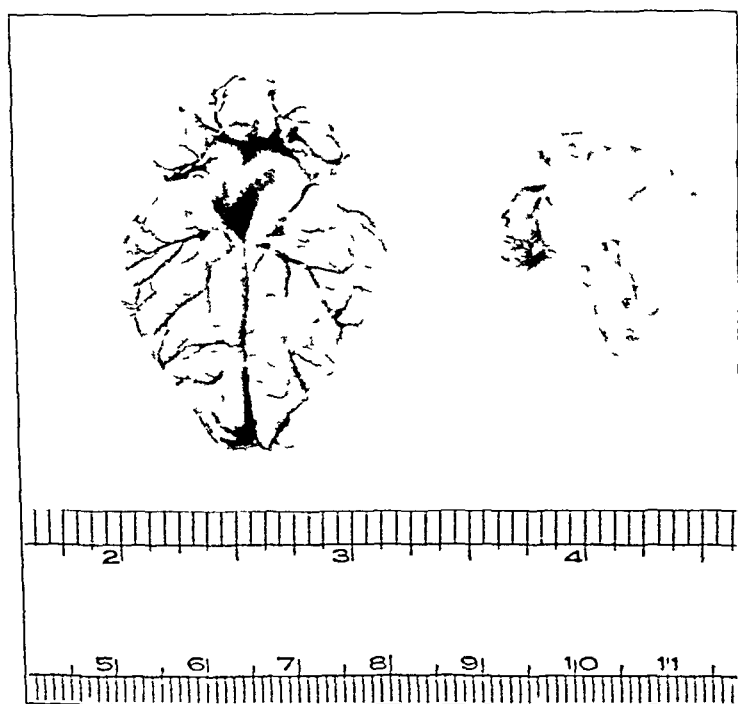


Fig 4—Displacement of the occipital poles and the anterior third of the vermis by an extradural-subdural tumor (rabbit DR 201), natural size

floor of the third ventricle could be seen bulging through the base of the brain. Coronal hemisection of the hemisphere disclosed the most extensive hydrocephalus observed in this series of intracranial growths (fig 4).

Five of the 10 animals with advanced subdural growths ranging in diameter from 9 to 14 mm exhibited clinical evidence of increasing intracranial pressure, and in 3 animals neurologic changes were demonstrated. Such changes included contralateral motor paresis and spasticity, anisocoria, questionable changes in the optic disks and nystagmus. As has been noted in the protocols, 1 animal showed a convulsive state, and a second exhibited the picture of persistent opisthotonos. Hydro-

cephalus was noted on gross examination of all 5 specimens. With this type of implantation the maximum period of growth compatible with the life of the experimental animal was somewhat longer than with the intracerebral type, ranging from forty to eighty-six days.

FURTHER STUDIES OF INTRACRANIAL GROWTHS PRODUCED BY EXTRADURAL IMPLANTATION

Fragments of papilloma were implanted extradurally in 9 additional animals. In the earlier study of tumors produced in this manner, two such implantations had resulted in small extradural growths after twenty-one and forty-two days, respectively. In the present series of animals, 5 showed no evidence of an extradural growth fifty-six to one hundred and thirty-three days after implantation. Two of the remaining animals had small extradural tumors, 3 by 4 mm., after forty-four and one hundred and nineteen days, respectively, and the third showed a larger tumor, 8 by 9 mm., fifty-four days after implantation. The fourth animal was found moribund in its cage fifty-two days after implantation. No neurologic examination could be made. An extradural tumor 15 by 12 by 7 mm. was found over area 17, greatly compressing the cortex, shifting the basal ganglions far to the opposite side and producing contralateral hydrocephalus. It is probable that the failure to secure successful implantation in the majority of animals and the comparatively slow rate of growth of the implants in the remainder (with a single exception) were due to the relative avascularity of the site of implantation.

SUMMARY AND CONCLUSION

The cutaneous papilloma induced in rabbits by the virus of infectious papillomatosis was transplanted intracerebrally in 5 of 8 animals. Massive tumors were produced in a large proportion of fourteen successful extradural and subdural implantations in 22 individual experiments.

Implants within the brain tissue exhibited a high rate of growth and expanded rapidly, in contrast to the more slowly growing extracerebral masses. The contrast was especially marked in the extradural implants, which increased in size exceedingly slowly and in many cases failed entirely to develop. These differences in rate of growth among implants in the three sites may possibly be attributed to the relative vascularity of the respective sites.

The clinical manifestations of increased intracranial pressure, the suggestive changes in the optic disk, the localized neurologic deficit, the extensive alteration in the form of the adjacent nerve tissue and the presence of hydrocephalus are findings in this particular experimental animal which are indisputably similar to those seen in human beings suffering from intracranial neoplasm.

SEVENTIETH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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LOS ANGELES

CONGENITAL DEFORMITIES

Early Diagnosis of Congenital Dislocation of the Hip—Fairbank¹ states that a normal anatomic result can follow congenital dislocation of the hip only when diagnosis is made early, i e, within twelve months. During this period, simple reduction of the dislocated hip will usually result in cure. When displacement of the femoral head is not great the following points on roentgen examination suggest congenital dislocation: shelving of the upper portion of the acetabulum, decrease in size of the center of ossification and displacement of the femur upward and outward.

Arthrography in Congenital Dislocation of the Hip—Severin,² at the Orthopedic Clinic in Stockholm, Sweden, has been able to outline the hip joint in roentgenograms by means of a solution of perabrodil (skiodan, sodium moniodomethane sulfonate). The material is injected into the hip joint with a modified lumbar puncture needle. From a study of the normal hip in 60 children from 1 to 13 years of age the author has

This report is compiled from a review of 151 papers selected from 223 titles concerning orthopedic surgery which appeared in the medical literature approximately between March 1, 1937 and July 1, 1939.

1 Fairbank, H A T. Brit M J 1 607, 1939.

2 Severin E. J Bone & Joint Surg 21 304, 1939.

observed that the acetabular lip lies 1 to 2 mm above the horizontal line through the Y-shaped cartilage, that the cartilaginous portion of the acetabulum should cover at least half the femoral head, that there should be only a small amount of contrast medium at the bottom of the acetabulum, and that the femoral head should be spherical. In hips which are subluxated a varying displacement of the head upward and laterally is observed, resulting in accumulation of a large amount of the contrast material in the bottom of the acetabulum. The acetabular lip is pushed upward, and the cartilaginous portion of the acetabulum covers less than half the femoral head. When complete dislocation of the femoral head has occurred, the acetabular lip is in normal position again. No irritation from injection of the material has been observed. Roentgenograms are taken immediately after the injection.

Skeletal Traction as a Preliminary Procedure for Congenital Dislocation of the Hip—Crego³ cites the following advantages for traction in treatment of dislocation of the hip. It avoids sectioning or removal of resistant soft parts, it avoids the use of the hip skid as well as the use of the considerable force which is required to lever the femoral head into place after the reduction can be effected, it avoids damage to the head, which frequently accompanies forcible closed manipulation, and it prevents the continuous intra-articular pressure which follows such reduction. The author describes a traction box. Stainless steel wires 0.08 inch (2 mm) in diameter were substituted for the usual Kirschner wire of the diameter of 0.0625 inch (1.5 mm). These wires are threaded on each end so that tension can be obtained by tightening ordinary bicycle spoke nipples on the ends of the wires against the bows. An ordinary trocar with a bore just large enough to admit the wire completes the necessary equipment. The technic consists of inserting the trocar directly through the soft part to the shaft of the femur, $\frac{1}{2}$ to $\frac{3}{4}$ inch (1.3 to 1.9 cm) proximal to the level of the adductor tubercle. The center of the shaft is located at this level, and the trocar is inserted through the bone and then through the soft parts on the other side. The wire follows, and the bow is attached. All this is done with sterile precautions. The patient is then put to bed on a Bradford frame, and traction is applied to the bow, the foot of the bed being elevated in order that the body weight may be used as countertraction. For children under 4 years of age the initial weight used is about 10 pounds (4.5 Kg). When roentgen examination shows the femoral head to be well down opposite the lower half of the acetabulum, the amount of traction is reduced so that there will be just enough pull to prevent upward displacement of the head, and this adjusted traction is maintained for ten days to two weeks longer. In several patients over 5

³ Crego, C. H., Jr. *J. Bone & Joint Surg.* 21: 353, 1939.

years of age it was necessary to tenotomize the flexor and adductor tendons of the hip and to use 20 pounds (9 Kg) of traction for as long as a month before the head had completely descended. If the acetabulum is too shallow or its roof too nearly vertical to permit permanent reduction or if closed reduction cannot be effected without an anesthetic, open operation is indicated. The author used skeletal traction as a preliminary procedure to either open or closed reduction in the cases of 27 children under the age of 7 years with posterior dislocation of the hip. In 11 cases the deformity was bilateral, making a total of 38 hips treated. Twenty-nine of these hips were reduced spontaneously without anesthesia. Nine were reduced by open reduction. The author eliminated 5 cases in which the patients were still in plaster at the time of writing and 5 in which there was femoral torsion, an inadequate acetabulum, or both, but of the remaining 28 the results were entirely satisfactory anatomically in 25.

Fracture Healing in Osteopsathyrosis Idiopathica—Sonnenschein⁴ reports an operation on each of 2 patients with severe osteopsathyrosis. The first was step approximation of the ends of a pseudarthrosis. Union was solid in ten months. In the second case there was marked anterior bowing of the tibia. A wedge resection was performed. Union was solid in four months. Sonnenschein observed that periosteal callus formed normally, although endosteal callus formation was delayed. He feels that one need not refuse osteotomy or surgical correction of pseudarthrosis in these patients.

NUTRITIONAL DISTURBANCES OF BONE

Citrates in Treatment of Infantile Rickets—Shohl and Butler⁵ report 2 cases of infantile rickets in which healing was induced by mixtures of citric acid and sodium citrate. They believe that this new form of therapy is a valuable adjunct to the accepted measures of treatment, especially in case of resistance to vitamin D therapy. They suggest that the new therapy may be applicable to other types of disorders of calcium and phosphorus metabolism.

DEVELOPMENTAL DISEASES

Endocrine Implication of Juvenile Chondroepiphysitis—A group of 259 patients 8 to 15 years of age with endocrine pathologic conditions were examined. Ninety-one, or 35.2 per cent, displayed evidence of single or multiple chondroepiphysitis (Köhler's disease, Legg's disease, Osgood-Schlatter's disease, Freiberg's disease). Eighty-five per cent of the 91 showed clinical or laboratory evidence of primary or secondary

⁴ Sonnenschein, A. *Zentralbl. f. Chir.* **65** 1970, 1938.

⁵ Shohl, A. T. and Butler, A. M. *New England J. Med.* **220** 515 1939.

hypothyroidism A control group of 99 patients without endocrine disease in the same age range included only 7 in whom there were chondroepiphyseal changes The authors⁶ concluded that chondroepiphysitis is of endocrine origin, specifically due to primary or secondary hypothyroidism, usually asymptomatic, and that chondroepiphysitis is a pathognomonic sign of hypothyroidism

[ED NOTE Chondroepiphysitis is in many cases associated with a physiologic disturbance in the complex endocrine system Sufficient evidence has not been presented however, to show hypothyroidism alone to be the cause]

TUBERCULOSIS

Paravertebral Aspiration of Tuberculous Abscess of Psoas Muscle—Warring and Kent⁷ advocate paravertebral aspiration of tuberculous abscess of the psoas muscle through the lumbar muscles They use a 5½ inch (13.9 cm), 15 gage needle for aspiration, local anesthesia having been induced along the path of the needle The needle is inserted 5 cm lateralward from the line of the vertebral spinous processes on the side of the abscess and at the level of the space between the third and the fourth or between the fourth and the fifth vertebral spinous process The needle is "directed slowly inward, parallel to the cross section of the body and slightly lateralward" Five aspirations were performed in 2 cases This method may be used before the abscess penetrates below Poupert's ligament The dangers of injury to contiguous structures are mentioned

Pulmonary Tuberculosis with Tuberculosis of Bones and Joints—Frank⁸ studied the incidence of pulmonary disease in a group of 1,003 cases of tuberculosis of bones and joints He found that in patients up to the age of 6 years there was often an association of these lesions Similarly, in the aged an osseous lesion was frequently associated with an active tuberculous lesion In the aged it was likely to be cavernous advancing tuberculosis However, between the ages of 10 and 30 the incidence of associated active pulmonary disease was rare Only 2.4 per cent of all patients showed a progressive exudative pulmonary tuberculosis together with an osseous lesion All other pulmonary lesions were benign The author strongly advises operative treatment of osseous foci despite the presence of corresponding lesions in the lungs He states the belief that removal of one tuberculous focus favorably influences the entire body

6 Schaefer, R. L., Strickroot, F. L., and Purcell, F. H. Endocrine Implication of Juvenile Chondroepiphysitis, *J. A. M. A.* **112** 1917 (May 13) 1939

7 Warring, F. C., and Kent, E. M. *Am. Rev. Tuberc.* **39** 338, 1938

8 Frank, H. *Beitr. z. klin. Chir.* **168** 337, 1938

OSTEOMYELITIS

Coccidioidal Osteomyelitis—McMaster and Gilfillan⁹ report 24 cases of proved coccidioidal granuloma of bone. Thirteen of the 24 patients died of pulmonary involvement. Two patients with pulmonary involvement survived. Four patients showed primary localization of the process in the synovia, in the others the condition was initially osseous. Multiple osseous lesions were more common than single ones. The importance of general as well as of local treatment is emphasized. In cases of acute involvement, with widespread lesions, conservative treatment by means of immobilization is advised. In cases of chronic involvement, surgical intervention, including incision and drainage, ankylosis of joints and even amputation has been employed. No medication has been found to be specific.

CHRONIC ARTHRITIS

Intermittent Hydrarthrosis—Berger¹⁰ reviewed the incidence and suspected etiology of intermittent hydrarthrosis and came to the conclusion that the condition is not a disease but an articular manifestation of a variety of general and local conditions. He reports a case in which the symptoms proved to be due to allergy. Elimination of the offending allergens from the diet caused disappearance not only of the concomitant allergic manifestations but of the hydrarthrosis.

BACK

Pain Low in the Back and Spina Bifida Occulta—Dittrich¹¹ made a study of 7 cases of pain low in the back. Four of the patients were males, and 3 were females. There was radiation of the pains, associated with congenital defects of the sacrum identified as spina bifida occulta. These defects consisted of oval to round defects in the sacral laminae, varying in diameter from several millimeters to centimeters and extending through the entire thickness of the lamina. These anomalies were accompanied by masses of fat and fibrous tissue in close contact with the nerve roots and so arranged that mechanical irritation of the nerves was produced. There were muscular tenderness, muscle spasm, limitation of motion in the back, disturbance of the deep reflexes, fatigue on exertion and more or less constant pain. Six of the 7 patients were relieved by laminectomy of the upper three sacral segments and removal of the fibroadipose tissue within the canal. In the seventh case the conditions found at operation were atypical and apparently beyond repair.

⁹ McMaster P. E. and Gilfillan C. Coccidioidal Osteomyelitis, J. A. M. A. 112: 1233 (April 1) 1939.

¹⁰ Berger H. Intermittent Hydrarthrosis with Allergic Basis, J. A. M. A. 112: 2402 (June 10) 1939.

¹¹ Dittrich, R. I. Am. J. Surg. 43: 739, 1939.

[**LEO NOTL** When spina bifida is present one frequently finds alterations in the size and position of the spinal articular facets which can through instability and later irritation, lead to pain in the lower part of the back]

NEOPLASMS

Synovial Sarcomas in Bursae and Tendon Sheaths—Berger¹² presents a comprehensive view of the subject of synovial sarcomas and publishes 4 case histories (with detailed microscopic observations) of synovial sarcoma originating in serous bursae and tendon sheaths. The lining tissue of the serous bursae and tendon sheaths is homologous with articular synovial membrane and consists of dense connective tissue through which are scattered polymorphous cells. It is composed of an outer vascular layer and an inner superficial layer containing dendritic cells. Three of the author's patients had synoviomas originating from serous bursae, two in the thigh and one in the axilla, the fourth had a tumor originating from the extensor tendon sheaths on the back of the wrist. Histologically these neoplasms are of a single tissue origin (mesenchymal) but present various morphologic modifications. The tissue consists of dense cellular masses giving rise to pseudoglandular, simple or ramifying cavities. The masses of cells are formed by branching, curved, sometimes polyhedral cells with a syncytial aspect. The histologic structure of the tumors in these 4 cases favors the conception that synovial tissue is a tissue *suu generis*, being in a broad sense part of the reticulohistiocytic system but unique in its pronounced endothelial potentiality. Synovial sarcomas are highly malignant tumors, although at first they seem to grow slowly. Synovial sarcomas of serous bursae apparently run a more rapid course than do those of articulations, and recurrences develop in almost all cases in which operation is performed. Death is generally due to pulmonary, exceptionally to cerebral, metastases. Cure may be obtained only by early amputation.

Hemangioma of Joints—Bennett and Cobey¹³ report 5 cases of hemangioma of the knee joint and give an account of 24 authentic cases previously reported in the literature. The cardinal points in the diagnosis of hemangioma are (1) intermittent pain and swelling present since early life, with or without a history of trauma, (2) no pain on motion, (3) slight limitation of motion, (4) presence of another hemangioma anywhere on the body (5) reduction in the swelling on elevation of the extremity, (6) negative results from laboratory and roentgen examinations, and (7) aspiration of blood from the joint. The treatment advised is excision for small pedunculated tumors and rest together with radium or roentgen therapy for nonpedunculated

12 Berger, L. Am J Cancer **34** 501, 1938

13 Bennett, G. E., and Cobey, M. C. Hemangioma of Joints. Report of Five Cases, Arch Surg **38** 487 (March) 1939

tumors In 1 case an attempt at excision was followed by hemorrhage and infection, and eventually amputation was necessary In another case complete excision was possible Radium or roentgen therapy administered after biopsy produced practically complete recovery in 3 cases In 4 cases the diagnosis was proved by biopsy In the fifth case the behavior of the process made the diagnosis probable

MISCELLANEOUS

Amputation Neuroma of Digital (Finger) Nerve—Josefsson¹⁴ reports 3 cases of neuroma of digital (finger) nerves causing severe pain which was incorrectly diagnosed as osteitis Neuroma often occurs when digital nerves are cut It is difficult to isolate the small digital nerve at operation The best treatment is dissection of the neuroma and removal of at least 3 cm of the nerve with the thermocautery

Roentgen Treatment of Gas Gangrene—Kelly and Dowell¹⁵ report 8 cases of gas gangrene treated by roentgen therapy, with recovery in 6 Two patients with involvement of the trunk died Through questionnaires to roentgenologists the authors were able to collect 132 cases of gas gangrene treated by roentgen therapy Of 105 patients with gas gangrene of the extremity 6 died Of 18 with involvement of the trunk 4 died Of 9 with diabetic and arteriosclerotic gangrene, 5 died The authors feel that roentgen therapy lowers mortality and lessens the necessity of amputation The earlier treatment is begun, the more easily the infection is controlled They advise administration of 100 r per port daily for three to five days

Dupuytren's Contracture—Smith and Master¹⁶ undertook a study to determine whether any relation exists between trauma and Dupuytren's contracture For subjects they chose upholsterers, who continuously use the palm Five hundred and thirty-six men who had worked at the trade for two years or more were studied Six cases (1 per cent) of Dupuytren's contracture were observed In these cases the disease occurred after twenty or more years in the occupation It was bilateral in all but 1 case No evidence of any hereditary influence was found This incidence is no higher than that found in other studies The writers do not regard Dupuytren's contracture as an occupational disease

FRACTURES AND DISLOCATIONS

Traction-Abduction for Fractures of the Arm—Heyl¹⁷ evaluates the results of the traction-abduction treatment for fractures of the arm

¹⁴ Josefsson, H Acta med Scandinav **81** 860 1939

¹⁵ Kelly, I T and Dowell D A Arch Phys Therapy **20** 88, 1939

¹⁶ Smith, K D and Master W E J Indust Hyg & Toxicol **21** 97 1939

¹⁷ Heyl, I H Fractures of Upper Extremity and Shaft of Humerus Arch Surg **38** 295 (Feb) 1939

There were 106 fractures of the upper extremity and shaft of the humerus, 17 fractures of the greater tuberosity, 46 fractures of the surgical neck and 3 fractures of the shaft. These fractures were treated at the Beckman Street Hospital, New York, from 1929 to 1934, by the various members of the staff. This method was used for fractures of the upper extremity of the humerus. It required long periods of hospitalization, and a review of the end results showed no advantage or need (with exceptions) of the use of this method for these fractures.

[ED NOTE: This method has its use in individual cases but should not be applied to all the fractures of the humerus under discussion. Whether this method is still used for these fractures is not stated.]

Operative Treatment of Dislocation of the Head of the Radius—Aside from the common so-called luxation of the radial head (which the French aptly call *pronation douloureuse*), isolated dislocation of the radial head is a comparatively rare lesion. It usually occurs in childhood. In adults it is often associated with fracture of the shaft of the ulna. Frequently the deep branch of the radial nerve is injured in the supinator canal. The dislocation is usually volar. While closed reduction may be attempted, the author's¹⁸ experience is that accurate reduction can be obtained only by open operation. The fibrous ring from which the head has slipped must be incised and the head replaced, after which suture is performed. When the head is reduced it stays well in position. The 3 cases reported emphasize the foregoing points. In a case in which operation was performed one and one-half years after dislocation, resection of the scarred ring and ligaments was necessary before reduction was obtainable. Extension of the elbow lacked 45 degrees at the termination of treatment in this case. Early recognition and operation are stressed.

Nonunion of Carpal Navicular Bone—MacCallow¹⁹ states the opinion that nonunion of the carpal navicular bone is the result of defective treatment, frequently of failure to recognize the presence of a fracture early. All injuries to the wrist with tenderness over the navicular bone should be treated by splinting, and roentgenograms should be taken in two weeks. Although a fracture may not be evident immediately after injury, it will be shown after two weeks. The splint, with the hand in dorsiflexion and radial deviation, should be worn for eight to twenty weeks, during this period vigorous use should be encouraged. When nonunion is found, splinting for six months may be tried, but this method is uncertain. The author has found that removal of the dead bone does not lessen disability. He advises cross drilling of the fragments and splinting for twelve weeks. In 13 patients with nonunion so treated, union has occurred.

18 Lotsch, F. *Zentralbl. f. Chir.* **37** 2038, 1939.

19 MacCallow, F. H. *M. J. Australia* **1** 391, 1939.

Treatment of Fractures of the Neck of the Femur—At the fourth Congress of the International Society of Orthopaedic Surgery and Traumatology, there was a symposium²⁰ on fractures of the neck of the femur. Dr Lothar Kreuz, of Berlin, Germany, stated that extra-articular nailing of true cervical fractures gives the best chance of avoiding hindrance to healing. It is the quickest, safest and most successful method for patients between the ages of 70 and 80. For adults up to 60 conservative treatment gives about the same end results. For children conservative treatment alone is indicated. Dr Sven Johansson, of Sweden, described his method of guiding a Smith-Petersen nail into the head of the femur after accurate reduction. This method he uses also for young patients. He states that satisfactory healing occurs in 90 per cent of the patients who survive. Dr Adam Cruca, of Poland, stressed the necessity of revascularization of the femoral head for healing of the fracture. He stated the belief that this is best aided by correct reduction and fixation with a nail. He reported 93.4 per cent of favorable late results by his technic of subcutaneous nailing. According to Dr Louis Tavernier, of Lyons, France, fractures are a mechanical and not a biologic problem. Correct reduction with extra-articular osteosynthesis gives good results in about 80 to 85 per cent of cases. Ten to 20 per cent of the patients later have chronic arthritis. For late pseudarthroses the author advises a transtrochanteric osteotomy. Drs Jose Valls and Enrique Logomarsino, of Buenos Aires, Argentina, distinguished between the treatment of recent fractures and that of old fractures. Extra-articular osteosynthesis is the best method for recent intracapsular fractures. They reported 82 per cent of good results, with a .4 per cent mortality. For old fractures of which a satisfactory reduction can be obtained, they recommend osteosynthesis. When good reduction cannot be secured, intertrochanteric osteotomy has given the best results.

Overtgrowth of Femoral Shaft Following Fractures in Childhood—An "end result study" of 59 fractures of the femoral shaft in children under 16 years of age was made by Aitken and his associates²¹. A film 4 feet (121 cm) long with a special cassette was used, with the child standing erect and the tube placed at a distance of 7 feet (213 cm) in order to obtain accurate measurements. The patients were divided into two groups: one composed of children 13 years of age or over and the other of children 12 years of age or under. There were 6 patients in the first group. The time since fracture averaged five years. In all these cases the fragments were either anatomically reduced or laterally displaced without shortening. In 5 there was an average shortening of 1 cm despite the fact that in none of these was there shortening on

²⁰ Intracapsular Fractures of the Femoral Neck. Compte rendu du Congrès International de Chirurgie Orthopédique, Berlin 1939.

²¹ Aitken, A. P., Blackett, C. W. and Cincotti, I. I. *J. Bone & Joint Surg.* 22: 334, 1939.

discharge. In the second group there were 44 children. In 7 of these the fragments were anatomically reduced. In 1 there was no difference in the length of the femur at the time of writing. In the remaining 6, the fractured femur was longer. The overgrowth averages 1.1 cm. Three patients were discharged with lateral displacement without shortening. These now show an increase in the length of the fractured femur averaging 0.6 cm. Twenty-nine patients were discharged from the hospital with complete displacement and overriding of the fragments. In 15 of these the femur on the fractured side is now longer than on the sound side. Nine of these were discharged with an average shortening of the femur of 1.2 cm, and the femur is now 0.4 cm longer than on the sound side. The remaining 6 patients were discharged with an average shortening of 0.6 cm. There were 14 patients who still showed some shortening. Eleven of these were discharged, with an average shortening of 1.3 cm. In each of these the fractured femur is still 0.5 cm short. This shows an average overgrowth from the position on discharge of 0.8 cm. In the entire series 29 patients discharged from the hospital with over-riding of the fragments, there was an average overgrowth of 1.1 cm. By way of summary, fractures of the femoral shaft in children between the ages of 13 and 16 years are apt to show eventual shortening, whereas fractures of the femoral shaft in children under 13 years of age in a great majority of instances show overgrowth of the femoral shaft.

Insufficiency Fractures of Femur and Tibia—Hansson²² reports 3 cases of callus formation along the long bones subsequent to slight trauma, with no fracture line visible. In each case there was local pain, worse on use of the limb. The author states the opinion that these fractures were due to overexertion to static overload. A similar picture is seen in cases of dietary deficiency. Such callus formation is sometimes mistaken for tumor formation.

Posterior Dislocation of Lower Femoral Epiphysis—Burman and Langsam²³ describe a rare injury, posterior dislocation of the lower femoral epiphysis, occurring during a breech delivery. The dislocation is associated with femoral subperiosteal hemorrhage which may show advanced ossification under the lifted periosteum in eight to eighteen days on the roentgenograms. In the writer's case two attempts at manipulation to replace the epiphysis were unsuccessful. The epiphysis was displaced posteriorly, laterally and proximally. At open operation the epiphysis was replaced. After this, manipulation was again resorted to, in order to correct a slight displacement. Roentgen examination approximately two months after birth revealed remodeling of the shaft.

²² Hansson, C. J. *Acta radiol* **19** 554, 1938.

²³ Burman, M. S., and Langsam, M. J. *Posterior Dislocation of Lower Femoral Epiphysis in Breech Delivery*, *Arch Surg* **38** 250 (Feb) 1939.

and central placement of the lower femoral epiphysis. Roentgenograms taken approximately nine months after birth revealed the epiphysis to be slightly tilted, the epiphyseal line somewhat irregular and the shaft narrowed but assuming an almost normal contour. The child was followed to the age of 14 months. The child walked well. There was a lack of 5 degrees of extension and a shortening of $\frac{1}{2}$ inch (1.3 cm.) in the involved extremity. Resumes of 3 previously described cases are recorded. It is the writer's opinion that manipulation or open reduction is not indicated, since nature itself remedies the defect.

Operative Treatment of Avulsion Fractures of the Eminentia Intercondyloidea—Confronted with an avulsed eminentia intercondyloidea in the knee of a 10 year old boy. Paas²⁴ resorted not to extirpation of the fragment or to attempts at obtaining healing by maintenance of extension but to replacement of the fragment. He accomplished this by drilling a hole from just above the tibial tubercle to the bed of the avulsed fragment. He then transfixed the fragment with a heavy silk suture and passed both ends of the suture down through the canal securing them externally in the substance of the patellar tendon. This held the fragment in accurate contact with its bed. Roentgenograms taken one and one-half years later reveal excellent union. The result was a normal knee.

[ED. NOTE. The method should be noted. It seems worth copying.]

Dislocation of Lisfranc's Joint—Jazikoff²⁵ reports 3 cases of dislocation at the tarsal-metatarsal joint and states that only 180 cases have been published in the literature. This is a rare traumatic lesion caused by direct and great violence and often accompanied by fractures of the metatarsal and tarsal bones and by rupture of vessels and ligaments. Treatment consists in attempts at closed reduction as soon as possible. Some authors report that reduction is very easy but Jazikoff agrees with those who find that in many cases reduction is incomplete owing to obstruction by fragments of bone and torn ligaments. Of 32 cases described in the Russian literature satisfactory reduction was obtained in only 11. There is a strong tendency to redislocation after reduction. Open operation is indicated only when the first metatarsal bone is dislocated, in order to free the interposed anterior tibial tendon. The prognosis should be guarded but with good reduction and no associated fractures the results are good.

Fractures and Fracture-Dislocation of the Astragalus—Miller and Baker²⁶ discuss fractures and fracture-dislocations of the astragalus presenting facts regarding anatomy, function, types of fracture and their treatment. A brief review of the literature is included. For fractures

²⁴ Paas, H. R. Arch. f. orthop. u. Unfall-Chir. **39** 51 1938.

²⁵ Jazikoff, D. Rev. d'orthop. **26** 126 1939.

²⁶ Miller, O. L., and Baker, L. D. South. M. J. **32** 125 1939.

of the neck and body with displacement the need for recognition and accurate replacement is stressed. For fractures with displacement of the fragments early open reduction is usually necessary to assure accurate reposition and to avoid aseptic necrosis. Incision in front of and behind the ankle may be necessary for accurate reposition of the fragments. In cases of damage to the cartilage of the subastragaloid joint and subsequent pain in the joint, triple arthrodesis is advised. At times panastragaloid fusion is necessary. Astragalectomy in adults as a means of improving the impaired blood supply in astragalar fractures is condemned. A tabulation of the type of fracture and of the end results in 30 cases of fracture of the astragalus is given.

Fractures and Pregnancy—Lampert²⁷ adds 4 cases to the rather small number appearing in the literature. In 3 the fractures were pelvic. In these, as in the reported cases, union was prolonged past the usual dates. In 1 of his cases a large exostosis existed on the pubis, the consequence of a fracture sustained four months before the patient became pregnant. During the succeeding pregnancy the exostosis was spontaneously absorbed, and a normal delivery ensued. The author agrees with the opinions expressed in the literature that bony union in maternal fractures is delayed during the first and middle thirds of gestation. During the last three months rapid bone formation occurs.

ORTHOPEDIC OPERATIONS

Tendon Transplantation in the Upper Extremity—Steindler²⁸ emphasizes the following principles for tendon transplantation: 1 Any contracture should be corrected in order that the limb may be passively brought through the range of motion without the slightest resistance. 2 The muscle selected should have a similar or related action. 3 The integrity of the muscle unit must be respected. 4 The transplanted muscle must have adequate power. 5 The tendon pull should be on a straight line. 6 The tendon should be transplanted under suitable tension. 7 The tendon should be anchored securely, preferably by periosteal or bony attachment or, if tendon to tendon attachment is carried out, by the buttonhole suture. 8 The gliding apparatus should be preserved. In discussing the application of tendon transplantation to the upper extremity, Steindler describes procedures to aid abduction of the arm, flexion of the elbow, extension of the wrist and fingers and opposition of the thumb.

End Results of Tendon Suture of Arm and Hand—Heck²⁹ considers the advisability of primary and secondary suture of severed tendons. He reviews the previous statistics and emphasizes the differ-

27 Lampert, J. Arch f orthop u Unfall-Chir 39 675, 1939.

28 Steindler, A. Am J Surg 44 260, 1939.

29 Heck, F. Arch f orthop u Unfall-Chir 39 21, 1939.

ence of opinion existing in well informed circles By far the largest series of tendon sutures is that reported by Zweigbergk, of Sweden (688 tendon sutures) In 65 cases of primary suture a good result was obtained (80 per cent of the extensor tendons and 45 per cent of the flexor tendons) In 35 cases of secondary suture 25 extensor tendon sutures eventuated in 22 good and 3 bad results The results of secondary suture of 7 flexor tendons were good in 6 instances and bad in 1 The author then presents his own series of 75 cases of injuries to the tendons of the hand observed at the Wurzburg clinic Primary suture was carried out on the extensors 31 times, on the flexors 23 times and on both 5 times There were good results with 64.6 per cent of the extensors and with 43.4 per cent of the flexors Secondary suture was carried out 16 times (8 extensors and 8 flexors) It was successful in 62.5 per cent of the extensors and in only 25 per cent of the flexors In general, the author prefers primary to secondary suture, which he reserves for tendon injuries with extensive soft tissue damage

Arthroplasty of the Hip—Instead of covering the reshaped surfaces of a joint with a membrane to prevent ankylosis, Smith-Petersen³⁰ uses an inert mold made of vitalium over the head of the femur in arthroplasty of the hip He describes his operative technic in detail, with excellent line drawings The incision is similar to that which he describes for acetabuloplasty Points in operative technic which deserve emphasis are 1 The utmost respect for anatomic structures should be observed Intrapelvic exposure of the acetabulum is preferable (occasionally reflection of the sartorius muscle from the anterior superior iliac spine is necessary) 2 Reflection of the origin of the gluteus muscles from the lateral aspect of the ileum should be done to facilitate dislocation of the hip 3 After the anterior capsule has been excised, any overgrowth of the head of the femur should be removed before dislocation of the hip is attempted 4 Complete removal of the anterior capsule and of the Y ligament of Bigelow is necessary to prevent excessive formation of scar tissue

Postoperative treatment consists of suspending the extremity in a Hodgen splint with a Pearson attachment At the end of the second week roller skating exercises are started A roller skate is attached to the back of the ankle, and the patient takes abduction-adduction exercises over a board which can be tilted to produce more or less resistance as muscular strength increases This is followed by exercise on a stationary bicycle and in a walker No end results are reported since the 29 patients for whom the vitalium mold has been used have all been operated on since June 1938

30 Smith-Petersen, M N J Bone & Joint Surg 21 269, 1939

Repair of Anterior Cruciate Ligament of Knee—Campbell³¹ gives the end results of repair of the anterior cruciate ligament of the knee joint. In 8 cases repair was done by the method of Hey-Groves, and in 14 cases the writer's technic was employed. The latter procedure was described in 1936. A strip of quadriceps tendon, capsule and patellar ligament 8 inches (20 cm) long and $\frac{1}{3}$ inch (0.8 cm) wide is obtained from the anteromedial aspect of the knee. This strip is left attached to its lower end and passed through a drill hole in the inner tuberosity of the tibia. It emerges at the tibial attachment of the anterior cruciate ligament and through a second drill hole in the external femoral condyle is fixed to the fascia lata or to the periosteum of the femur. The operations were performed on patients between the ages of 18 and 25 years. There were excellent results in 13 cases, in 2 the results were poor and in 7 the patient could not be followed. The medial semilunar cartilage was removed in 18 cases, the external, in 1. The author expresses the opinion that independent rupture of the anterior cruciate ligament causes definite disability and must be repaired to secure maximum function.

Surgical Treatment of Spastic Paralysis—This study by Heyman³² was based on 280 operations on 176 patients. The patients selected for operation were from a group of approximately 1,500. Surgical treatment was considered merely an adjunct to a broad therapeutic regimen. The value of motor nerve branch resection of the internal popliteal, obturator and sciatic and the external popliteal and median nerves is discussed in detail. The operation is considered of great value for the lower extremity and of limited value for the upper. Tendon transplantation and arthrodesis of the wrist did not disclose any single satisfactory method of improving the spastic hand. The most satisfactory results followed arthrodesis of the wrist combined with crossed tendon transplantation to the dorsum of the wrist or the finger extensors. Transplantation of the hamstring tendons with the patella to reinforce the quadriceps was less successful than transplantation of the insertion of the patella tendon downward. Arthrodesis of the subastragalar region was successful if accompanied by proper tendon transplants.

RESEARCH

Experimental Bone Sarcoma—Hellner³³ describes the development of bone sarcomas in the growth area of rabbits' knees after exposure to radium for one and one-half to two years (3 sarcomas in 5 animals). He does not use the radium-petrolatum plug in the medulla, as some workers have done, but uses external irradiation. In a series of 8

31 Campbell, W. C. South M. J. **32** 442, 1939.

32 Heyman, C. H. Surg., Gynec. & Obst. **68** 792, 1939.

33 Hellner, H. Beitr. z. klin. Chir. **168** 538, 1938.

animals he combined irradiation with the production of a suppurative staphylococcic arthritis. One animal of this group had a sarcoma. He states the belief that infection neither expedites nor delays the development of a bone sarcoma due to radium. The rays exert a specific sarcoma-evoking action, particularly on areas where increased new cell formation is in process.

Growth in Length of Vertebrae—Haas³⁴ carried on experiments in dogs to demonstrate that growth in length in the vertebrae takes place by proliferation at the epiphysial cartilage plate. Markers were placed in the epiphyses and in the body of one vertebra, and another marker was placed in an adjacent vertebral body. Roentgenograms taken after one hundred and twelve days and compared with those taken at the beginning of the experiment revealed that markers in the same body were not any farther apart. The markers in the epiphyses had separated from each other, from those in the bodies and from that in the adjacent body. These experiments are similar to those of John Hunter, who demonstrated the same fact in the long bones. As yet this fact has not been shown to hold for growth in length in the vertebrae of man.

Peripheral Circulatory Disturbances in the Development of Osteoarthritis—Kling³⁵ studied the joints and blood vessels in 13 cases of amputation for gangrene following chronic disease of the peripheral blood vessels. He found the lesions of osteoarthritis not more extensive or frequent than in a group of persons of similar age with normal peripheral circulation. Pronounced osteoarthritis was present in only 2 instances. In severe arteriosclerosis the synovial vessels were involved less than were vessels elsewhere.

Role of the Three-Flanged Nail as a Foreign Body—Felsenreich³⁶ studied sections of the neck obtained at varying dates after nailing and reports the evidence obtained as pointing to the value of the method. He has studied the foreign body aspect. In a section observed nine weeks after nailing the contiguous lamellas about the nail were walled off from the nail by newly forming bone. Uniformly (even with the most satisfactory brands of stainless steel), rest forms, and rust granulomas regularly form. They are of interest but seem in no way to hinder bone formation in the fracture area. After removal of the nail they are absorbed. The canal in which the nail lay was replaced by connective tissue and eventually by bone. The three pigments observed in the rust granulomas disappeared histologically. The reaction of bone in the neck of the femur to a foreign body is somewhat different from that of bone in the long shafts.

³⁴ Haas, S. L. Growth in Length of Vertebrae, Arch Surg 38 245 (Feb) 1909.

³⁵ Kling, D. H. Am J M Sc 197 358, 1939.

³⁶ Felsenreich, F. Arch f klin Chir 194 584, 1939.

Obituaries

HARVEY CUSHING, M D

1869-1939

The bare facts of the life of Harvey Cushing may be found in many places, but it will be some time before words can be written which will convey the complete picture of this man, who was surgeon, author, artist, bibliophile, soldier and scientist

There was a great similarity in many respects between his life and that of Sir William Osler, and there are those who believe that Cushing deliberately patterned his thoughts and mode of life after that great physician. Cushing, however, was too great an individualist to carry his idealization of a character to the point of aping him and would have denied vehemently that he had ever looked at Osler with anything but a respectful and admiring critical eye. Nevertheless, his membership in that informal group of chosen young men in Baltimore, the "latch-keyers," who had free access to Osler's home and thereby were exposed to the informal, affectionate discourses given on great men and books in medicine and to the stimulating prods delivered in an apparently casual manner had a profound effect on Cushing's character. It was through the pages of his Pulitzer prize-winning biography that a younger generation came to know Osler, and it was when Cushing was discussing "the chief" that he exhibited his greatest charm. Some day the affection, admiration and respect which he bore his older brother, Edward, will be brought to light. A few of his more intimate young associates were told of the bonds which united him to "Ned," entirely dissimilar though they were in every way. Try as hard as he might, the younger man could never exhibit the infinite patience, tolerance and camaraderie displayed by his brother. It was in his nature, but it was inhibited by a driving ambition to reach perfection.

One often wonders what the procession of thoughts was in the mind of the young doctor who had just completed his surgical residency when he asked for the privilege of devoting his future to surgery of the nervous system on the staff at Johns Hopkins Hospital. A glimpse is given in his story of "Neurological Surgeons," when he tells briefly of the hours of study and effort spent at the bedside of an unfortunate Negro who had been paralyzed by a bullet lodged within the spinal canal. It is difficult for physicians of the present generation to realize that it was necessary for him to crank the machine to generate enough current to obtain the roentgenogram by which the level of the bullet was located. This persistence and attention to detail had been manifested at

an earlier period in the meticulous records which he had kept of his patients when he was an intern at the Massachusetts General Hospital. Free hand sketches which illustrated the salient points in the findings at physical examination or at operation gave originality and character to his notes, and when, after a friendly bet with a fellow house officer as to



HARVEY CUSHING, M.D.
1869-1939

which one could administer ether without causing the patient to vomit, he kept an accurate graph of the pulse rate and respirations, it was the first such record and the forerunner of the more elaborate "anesthesia charts" used today. This desire to attain perfection in whatever he undertook was the motivating force which characterized Cushing's professional life. An operation was either good or bad. There was nothing between

A stern and unrelenting taskmaster, he was no less demanding of his own time and physical and mental effort than of those of his associates. Those who have seen him sitting beside a patient recently operated on, aiding in the details of the nursing, have realized how concentrated was his interest in the patient's future. It was his desire to know more than the details of the patient's illness, there were the patient's personality, occupation, ancestors, domestic life, avocation and other items, which others might consider trivial, to be included in the balanced picture which made of the patient a surgical problem. To wrestle with that problem from the beginning to the end and not be merely a middleman surgeon, to "keep score" on his own efforts with self-searching honesty, to profit by the judgment which comes from recognizing and considering mistakes, was a game, which he often compared to golf. According to Cushing, every surgeon should be always striving to better his own past.

An ugly scar left by an osteoplastic craniotomy was the sign of a poorly performed operation, though the tumor had been removed and the patient had been socially and economically restored. The artistry of his operative procedures, admittedly time consuming, could never be understood or appreciated by the surgeon who believed that a successful surgeon must be a "minute man." Cushing taught that the advancement of neurosurgery depends on the exactness and care with which the more mechanical portions of surgical technic are carried out, leaving no opportunity for a failure when precision might have prevented it. Yet it was interesting to hear of the horror and skepticism with which he viewed the operations performed by Halsted when he first went to Johns Hopkins from his internship. He had been accustomed to see an amputation of the breast performed in twenty-eight minutes by the clock, and a lengthy period of anesthesia was looked on as an almost insurmountable obstacle to recovery. He looked with misgivings on the instructions to leave an operative wound alone for several days before it was dressed, and the use of silk sutures and ligatures was entirely beyond his experience. But to Cushing, preeminently of Halsted's pupils, must go the credit for adopting a technic which he learned to be scientifically correct and for spreading its gospel throughout the surgical world. One has only to look at the record of his operative statistics in a field in which he was pioneering to be convinced of the soundness of his practice.

Born in the Midwest, in a part of the original Northwest territory and one of a succession of physicians he lived the greater part of his life in the East, but his interest in surgical happenings beyond the Alleghenies was genuine and sustained. He had an enthusiastic curiosity for the "feel" of a city or an institution which he was visiting. His companions were plying with questions, often embarrassing, as they dis-

played the native son's ignorance of matters about which he should have known. In the end both profited, the one by adding to his store of knowledge, the other by having his interest stimulated in a subject which until then had been wholly unexplored.

Cushing's many contributions to literature are evidence of his masterful and individualistic style of writing. As with all great authors his literary efforts were attended by considerable agonizing until the final form represented perfection as nearly as he could reach it. Whether in the operating room, on the tennis court, in the preparation of a paper or in the presentation of a subject before a medical meeting, Cushing was exacting of his young associates. Often it was difficult for the younger men to look on these disciplinary measures as anything but sheer mental or physical cruelty, but when years later, they received a short note saying, "More power to your elbow. H. C.," understanding came. His love for books was encouraged by Osler, and he in turn used the contents of his own library to arouse the interest of a prospective bibliophile. Old books, as unexpected gifts, often sowed a seed in the recipient and thus brought to Cushing a harvest of delight.

It is always difficult to realize that such a dynamic personality has passed. During his lifetime, at home and abroad, he received innumerable tributes to his genius with what at times seemed to be a studied indifference. But there were always words of appreciation for even the simplest of these recognitions of his achievements at the right moment. Eventually the surgical world will come to know him as a great physician and, for himself, Dr. Cushing would have considered that the highest praise.

LOYAL DAVIS, M.D.

Notices

SPECIAL ISSUE IN HONOR OF DR DEAN LEWIS

Preparations are being made for a special number of the *ARCHIVES OF SURGERY* in honor of the sixty-fifth birthday of Dr Dean Lewis, who has been the Chief Editor of the periodical since its publication was begun. While it is impossible to give a definite date of publication, since the material is not yet in the hands of the publisher, the issue may be expected to appear in the next volume.

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6 If the valves in both the long and the short saphenous vein are incompetent, the varices will not collapse until two tourniquets are used, one being placed around the upper part of the thigh and the other just below the knee

7 If the varices are due to mere dilatation of the venous walls without valvular incompetence, the degree of collapse will be about the same with or without the tourniquet in place

The elastic bandage test for patency of the deep veins is performed by applying an elastic bandage from the toes to the upper part of the thigh and having the patient walk for several hours. If the deep veins are obstructed the patient will complain of an aching or cramping pain in the extremity. If no pain develops, the deep circulation is unobstructed. The development of pain is caused by acute passive congestion in the extremity. This test will often be the last resort in differentiating between incompetency of the communicating veins in the leg and obstruction of the deep veins

DIFFERENTIAL DIAGNOSIS

The conditions to be differentiated from varicose veins include the following: femoral hernia, arteriovenous aneurysm, lymphocele, muscle hernia, thromboangitis obliterans, peripheral arteriosclerosis, Raynaud's disease, diabetic neuritis, erythema induratum, Morton's disease, pes planus, rheumatic pains in the joints, sciatica, tabes dorsalis, ostitis, periostitis and menopausal arthritis. Varicose veins may be associated with any of these conditions, and the symptoms may be attributed to the varices even though the other condition is actually responsible. It is therefore necessary to secure a thorough history, a complete physical examination and adequate tests of the blood and urine as well as a careful evaluation of the arterial system in all cases in which there are symptoms suggestive of varicose veins

TREATMENT

The active treatment of varicose veins includes the injection of sclerosing solutions, high ligation of the saphenous trunks, excision of large masses of varices and ligation of the communicating veins. The aforementioned procedures are used singularly or in combination. Varicose ulcers are healed by relatively conservative measures before the more radical procedures are undertaken.

Patients with obstruction of the deep veins with compensatory dilatation of the superficial veins receive no active therapy until the obstruction is removed or disappears. If the obstruction is due to recent or persistent thrombophlebitis, the deep venous channels will not become

sufficiently recanalized to allow treatment in less than one year. In some cases recanalization never occurs.

Patients who have only incompetent valves of the long saphenous vein usually receive complete relief from high ligation of the vein. It is essential that the long saphenous vein be ligated flush with the femoral vein and that all superficial veins entering the saphenous fossa be interrupted. Occasionally a sclerosing solution is injected distally into the long saphenous vein at the time of the ligation. For this group of patients, however, it is preferable to delay injections until two to six weeks postoperatively in order to allow the dilated veins to recede in size as much as possible. Large saccular dilatations along the course of the saphenous trunk are excised at the time of the high ligation.

When incompetency of the valves in the long saphenous and communicating veins of the thigh exists, high ligation of the saphenous and simultaneous ligations of the communicating veins are performed. After the patient becomes ambulatory a sclerosing solution is injected into any residual varices.

If the valves in the long saphenous vein and in the communicating veins of the leg are incompetent, these vessels are ligated flush with the deep veins. In order to secure deep ligation of the communicating veins of the leg the modified Madelung, or flap, operation⁵ is indicated. The patients in this group are the ones who most often present brawny edema and intractable ulcers.

If the varices are due to incompetent valves in the communicating veins of the thigh and the valves at the femorosaphenous junction are intact, ligation of the affected communicating veins is indicated, and if small varices persist postoperatively, they are treated by injection after the patient becomes ambulatory.

Patients with secondary dilatation of the short saphenous vein due to back pressure through an anastomotic branch from a varicosed long saphenous trunk are usually relieved by high ligation of the saphenous vein and subsequent injection treatment of persistent varicosities.

A varicose condition of the short saphenous vein alone is treated by injections if the varicosities are small. When the varicosities are large, ligation of the short saphenous vein flush with the popliteal vein is performed. Subsequent injections may also be used for persistent varicosities.

Incompetence of the valves in both saphenous veins is treated by high ligation of both venous trunks.

Incompetent communicating veins of the legs without involvement of the saphenous trunks are treated by ligation of the affected veins flush with the deep veins.

⁵ Faxon H. H. Present Method of Treating Varicose Vein. *New England J. Med.* **216**: 527-534 (Feb. 25) 1937. Boston.

Dilatations of the superficial veins without valvular incompetence are treated by injections.

During early pregnancy active therapy is justified. Patients in the third trimester of pregnancy, patients with active or recent phlebitis and patients with serious debilitating diseases are treated conservatively.

The sclerosing injections are always carefully and aseptically administered in order to avoid thrombophlebitis, local abscesses or septicemia. If the sclerosing solutions are injected outside the veins, sloughing and ulceration may occur.

The most serious complication of injection therapy is pulmonary embolism. Two patients have died of emboli at the University Hospitals. Both were kept in bed for ten days after the injections. It is essential that all patients remain ambulatory after the injections to avoid this catastrophe.

Excessive amounts of the sclerosing solutions have caused marked toxic reactions. In 1 of our patients, who received 12 cc of a 5 per cent solution of sodium morrhuate at one sitting, toxic hepatitis with jaundice and a high fever developed. The deep veins may be thrombosed by massive doses of the sclerosing solutions. Severe allergic reactions with marked collapse or even death of the patient have been reported.⁶ Hematuria has been observed to follow large doses of hypertonic solution of sodium chloride.

The fatty acid derivatives have proved to be the safest and most efficacious solutions for injection. Sodium morrhuate is the most widely used. At the University Hospitals the maximum dose for one sitting is 5 cc of the 5 per cent solution. Other effective fatty acid preparations are monoethanolamine oleate (monolate), sodium ricinoleate, potassium oleate, sodium gynocardate and sylvasol.⁷

Operating room technic is used for the ligation and excision procedures, which carry about a 2 per cent risk of major wound infection and a 0.3 per cent risk of pulmonary embolism.⁸ No patient has died after any of the operative procedures at the University Hospitals.

The patient may remain ambulatory after high ligations of the saphenous vein, but great care is always exercised postoperatively to prevent infection of the wounds. Most patients treated by means of multiple ligations or excisions remain in bed until the wounds are suffi-

6 Johnson, G. S. Recent Advances in the Treatment of Varicose Veins. *Surgery* 2: 943-965 (Dec.) 1937.

7 Sylvasol (G. D. Searle & Co.), formerly known as sylvasol, is a 5 per cent solution of the sodium salts of certain of the fatty acids of the oil extracted from a seed of the psyllium group.

8 Faxon, H. H., and Barrow, D. W. The End Results of High Ligation and Injection in the Treatment of Varicose Veins, *Surgery* 3: 518-527 (April) 1932.

ciently healed for the skin sutures to be removed. After the skin sutures are removed, Unna's paste boots^{8a} are applied. These are worn for seven to twenty-one days.

Recurrence of the varicose veins in less than one year occurs in from 10 to 25 per cent of even the most favorably treated patients.⁹ Our experience confirms this. Three factors account for most of the recurrences in the patients treated at the University Hospitals: (1) failure to ligate all the important "blow-out" vessels flush with the deep veins, (2) failure to excise large saccular masses of veins, and (3) failure to complete the treatment by injections into all the varices which persist postoperatively.

All patients are encouraged to return for periodic examinations and for treatment of the varices that may persist or recur after the primary therapy.

SUMMARY

A classification of varicose veins is presented for use in treating this disease.

A resume of the various diagnostic tests for varicose veins is given. The tests are interpreted with reference to the possible variations in venous incompetency.

The differential diagnosis of varicose veins is emphasized.

The selection of patients and the indicated therapeutic procedures are discussed.

The rules for avoiding the more important complications are emphasized.

8a The formula for Unna's paste is as follows: gelatin, 150 Gm., glycerin, 400 Gm., water, 350 Gm., and zinc oxide, 100 Gm. The first three ingredients are melted together, and zinc oxide, previously rubbed with a portion of the glycerin, is added. The boots are made by soaking loosely rolled 3 inch (7.5 cm.) cotton bandage in the melted paste. The extremity is bandaged from the base of the toes to the middle of the thigh. Five to seven layers of the gauze will give satisfactory support. After the boot has dried for twenty to thirty minutes the surface is powdered with talcum.

9 Ferguson, L. K. Ligation of Varicose Veins. Ambulatory Treatment Preliminary to Sclerosing Injections, *Ann Surg* **102**: 304-314 (Aug.) 1935. McPheters, H. O. The Present Status of the Management of Varicose Veins, *Surg, Gynec & Obst* **67**: 494-498 (Nov.) 1938. de Takats, G. Varicose Veins, in Christopher F. A. A Textbook of Surgery, Philadelphia, W. B. Saunders Company, 1936, p. 168. Johnson⁶. Faxon and Barrow⁵.

NERVE ACTION POTENTIALS IN EXPERIMENTAL TRAUMATIC SHOCK

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The role of the nervous system in the production of shock in the experimental animal has been emphasized by Slome and O'Shaughnessy,¹ who stated ^{1a} "The initial depressor effect of trauma is due to fluid loss, the significant secondary decline to shock is caused by the continued and continuous discharge of nervous impulses from the traumatized area. The nervous factor operating alone can cause death." These experiments have been discussed by Blalock and Cressman.²

Direct evidence for a nervous factor was adduced by O'Shaughnessy and Slome^{1a, c} by comparing records of the action currents in the nerves to a traumatized limb before and after trauma with those of the action currents in the nerves to the untraumatized control limb of the same animal. They stated ^{1a}

No abnormal impulses are recognizable for three quarters of an hour to one hour after trauma, after this time an almost continuous barrage of impulses is rapidly developed. These can be shown to be centripetal afferent impulses by ligaturing, sectioning or novocainizing the nerves peripheral to the electrodes. The absence of any impulses for a period after trauma, and their appearance after this time and persistence till death of the animal, accords accurately with the gradual decline of blood pressure which sets in at this time.

Only two illustrative records of such impulses are shown, one in each article,^{1a, c} without a description of methods used to record the nerve action potentials. However, some conclusion may be drawn regarding

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Aided by a grant from the Division of Medical Sciences of the Rockefeller Foundation

1 (a) Slome, D, and O'Shaughnessy, L. The Nervous Factor in Traumatic Shock, *Brit J Surg* **25** 900, 1938 (b) O'Shaughnessy, L, and Slome, D. Etiology of Traumatic Shock, *ibid* **22** 3, 1935 (c) Slome, D. Traumatic Shock, *Proc Roy Soc Med* **28** 73, 1935

2 Blalock, A, and Cressman, R. Experimental Traumatic Shock. Further Studies with Particular Reference to the Role of the Nervous System, *Surg Gynec & Obst* **68** 278, 1939

the amount of amplification employed by comparing the resting discharge with the discharge produced in response to tactile stimulation^{1c}

PURPOSE OF THIS STUDY

The experiments reported here were undertaken in an attempt to verify the existence of a barrage of impulses in experimental traumatic shock as reported by O'Shaughnessy and Slome and to determine, if possible, the origin of such a barrage and whether it is a causative factor in shock or is related to the low blood pressure, vasoconstriction and other changes which are a part of shock

METHOD

Action potentials of the nerve studied were amplified through a resistance-coupled amplifier operated by alternating current, and connected to a dynamic speaker type of oscillograph. The deflections were recorded on moving bromide paper. Amplification through this system was adjusted to give a deflection of about 1 cm from the base line in response to light stroking of the skin when the saphenous nerve was used or to muscle stretch by flexion at the knee in the case of muscular branches of the femoral nerve. The femoral nerve was exposed below the inguinal ligament, and records were made from the isolated saphenous nerve or from a portion of the muscular branches to the quadriceps muscle. Silver electrodes with an interelectrode distance of 5 mm were used, the nerve was kept moist with saline solution on cotton pledgets in the interval between recordings. In nearly all cases the intact nerves were used, but occasionally nerves were sectioned proximal to the electrodes to assure elimination of centrifugal action potentials.

Cats weighing 1700 to 3,500 Gm were used in all experiments. They were anesthetized with chloralose (a preparation of chloral hydrate and dextrose), 80 mg per kilogram of body weight, given intravenously in most of the experiments. In a few cases pentobarbital sodium, 25 mg per kilogram, was used. One carotid artery was exposed for the intermittent recording of blood pressure by a large needle connected to a mercury manometer. Continuous recording with a kymograph was unsatisfactory because of clotting and the resultant loss of blood in washing out the system.

After exposure of the nerves and the carotid artery in the anesthetized animal, a control tracing was taken from the nerve of each hind leg to obtain the response to touch or stretch and the base line of spontaneous electrical activity in the nerve before trauma. One thigh was then traumatized as described by O'Shaughnessy and Slome^{1a} by twenty blows with an iron bar, the femur being broken in about half the cases. Records were taken from the traumatized and from the control side within five minutes and at intervals of fifteen to thirty minutes thereafter to demonstrate both the spontaneous electrical activity and the sensory response of the nerves in both legs. In animals in which the femur was broken it was not possible to record the stretch response in the muscular branch after trauma.

Loss of fluid into the traumatized extremity was measured by the method described by Blalock,³ that is, comparison of the weight of the traumatized and untraumatized legs and expressing the increase in weight of the traumatized leg as per cent of total body weight

CONTROL RESULTS

Records were made of the action currents in the saphenous nerve of one leg and a muscular division of the femoral nerve in the opposite leg for periods of six and one-half to nine hours after the administration of chloralose to 4 cats. Records from the muscular division in 1 experiment showed a slight increase in spontaneous impulses for a short period four hours after the start of the experiment. In the other experiments there was no alteration in spontaneous activity or sensory response in the saphenous or muscular divisions.

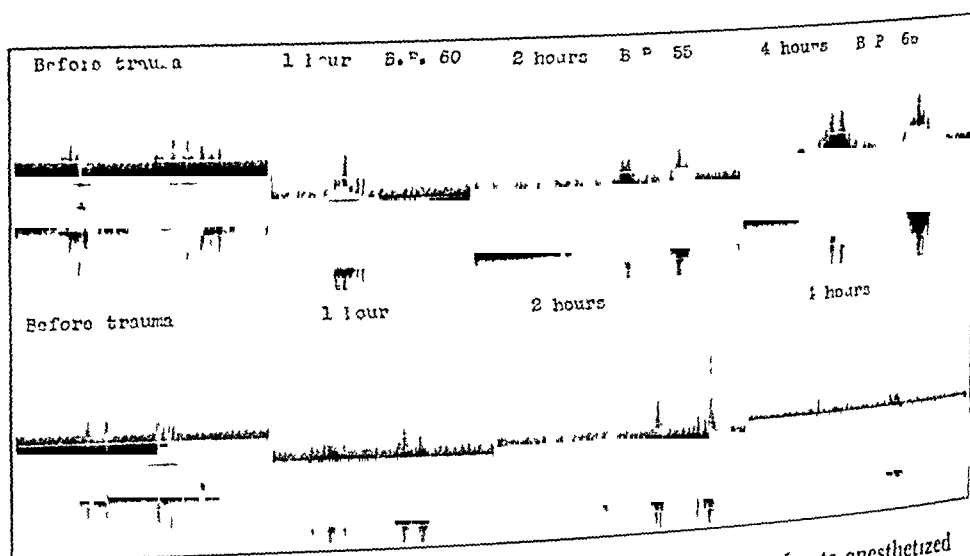


Fig 1—Record of nervous activity in the saphenous nerves of cats anesthetized with chloralose and subjected to trauma. The record for the traumatized extremity before trauma and one, two and four hours after trauma is shown at the top of the figure. The response to stroking of the thigh is shown in each record. Note the level of resting activities between responses. The record for the control (untraumatized) extremity at the same intervals is shown at the bottom of the figure.

EXPERIMENTAL RESULTS

GROUP 1 (saphenous nerves, chloralose anesthesia, trauma to thigh)—In 11 6 cats in this group of experiments, the fluid loss into the traumatized leg was from 12 to 3 per cent of the body weight, with the average 24 per cent. In 4 of the experiments there was no change in electrical activity in the nerves after trauma (fig 1), while in 2, increases were seen. In 1 this occurred one and one-quarter hours after trauma, when the blood pressure had fallen to 100 mm.

³ Blalock, A. Experimental Shock. Cause of Low Blood Pressure Produced by Muscle Injury, Arch Surg 20 959 (June) 1930

of mercury. The increase was rather slight and was equal on the traumatized and on the control side. In the other there was an increase on the control side only four hours after trauma, when the blood pressure was 65 mm. of mercury.

GROUP 2 (muscular branch of femoral nerve, chloralose anesthesia, trauma to thigh)—In the 13 cats in this group the loss of fluid into the traumatized leg varied from 19 to 32 per cent, averaging 24 per cent, of the body weight. Six cats showed no change in nerve activity, 7 showed slight to marked increase in activity, both in spontaneous discharges and in response to stretch. In 2 of these experiments the increase was greater on the traumatized side, in 1 it was greater on the nontraumatized side (fig. 2) and in the remaining 4 it was equal on the two sides (fig. 3).

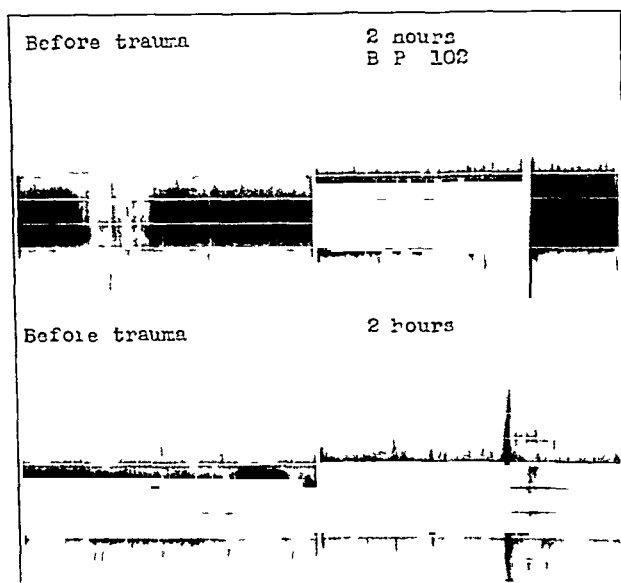


Fig. 2—Record of nervous activity in muscular branches of the femoral nerves of cats anesthetized with chloralose and subjected to trauma. The record for the traumatized extremity before trauma and two hours after trauma is shown at the top of the figure. Response to stretch is shown in each record, as well as resting activity. The record for the control extremity is shown at the bottom of the figure.

Of the 7 experiments in which there was any increase in the level of electrical activity in the nerves following trauma, in 3 this change began within five minutes after trauma and continued for the duration of the experiment. In 2 heightened activity was first observed two hours after trauma, and in the remaining 2 three hours after trauma. At the time the increased activity was first noted, the mean blood pressure varied from 88 to 125 mm. of mercury.

Of 3 experiments in which pentobarbital sodium was the anesthetic, there was an equal increase in activity in the nerves of both legs in 1, beginning two hours after trauma, when the mean blood pressure was 120 mm. There was an increase

in activity in the nerve in the control leg in 1, beginning one hour after trauma, at which time the mean blood pressure was 74 mm of mercury, and in the remaining instance there was no change aside from impulses which immediately followed the trauma and which were accompanied by twitching of the muscles

GROUP 3 (saphenous nerve and muscular branches of femoral nerve, chloralose anesthesia, shock by hemorrhage) —To determine if possible whether the increase in spontaneous nerve impulses seen in both traumatized and nontraumatized extremities was related to the anoxemia succeeding low blood pressure and peripheral vasoconstriction, shock was induced in anesthetized cats by removal of blood from the carotid artery in 6 experiments. To reduce the blood pressure below 80 mm of mercury, blood in the amount of 25 to 35 per cent of the body weight was gradually removed in one and a half to three hours. Loss of this amount of blood leads to death within three to six hours, often soon after the blood pressure

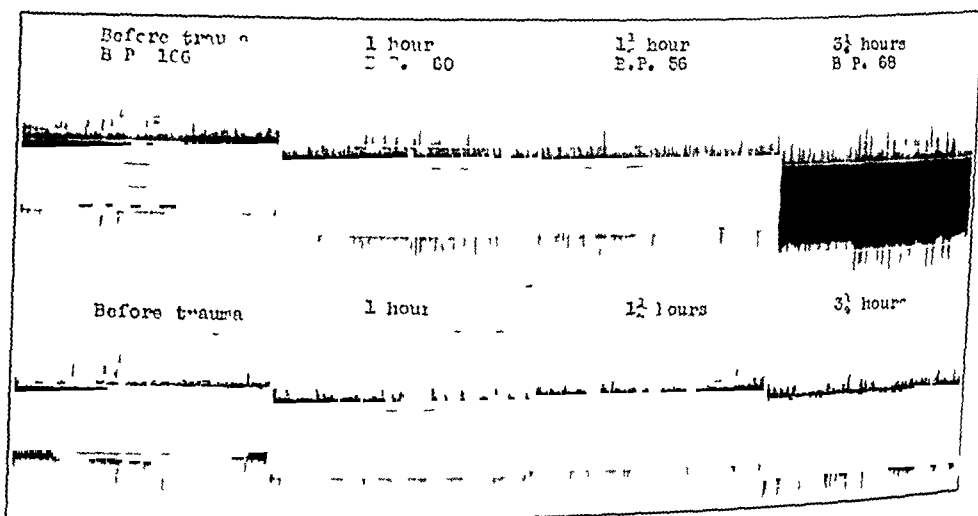


Fig 3—Record of nervous activity in muscular branches of the femoral nerves of cats anesthetized with chloralose and subjected to trauma. The record for a nontraumatized extremity before trauma and one, one and one-half and three and one-quarter hours after trauma is shown at the top of the figure. The stretch response as well as the resting discharge is seen in each record. The record for the traumatized extremity at the same intervals is shown at the bottom of the figure. The stretch response is seen only in the first record. The increase in resting activity is about equal on the two sides.

reaches shock level. In 4 cats no change in nerve activity occurred in either the saphenous or the muscular branch. In 1 there was a slight transient increase when the blood pressure was 80 mm of mercury, and in the remaining one there was a marked increase in spontaneous activity and response to touch and stretch after the blood pressure had been reduced to shock level.

GROUP 4 (trauma to isolated muscle) —In 3 experiments a single muscle of the quadriceps group of the thigh, with its vascular and nerve supply, was isolated and its record action potential changes when this single muscle was traumatized. In

cult in maintaining conduction in the nerve after trauma to the muscle caused abandonment of this line of attack.

GROUP 5 (anemic limb)—O'Shaughnessy and Slome^{1a} in cross circulation experiments rendered a leg anemic, believing such a leg to be anesthetic. To determine whether such anemia would result in increased or absent nerve action currents, anemic limb preparations were made in 4 cats by ligating the aorta, the ilio-lumbar artery, the middle sacral artery, the external iliac artery, the profunda femoris artery and the femoral artery and its branches in the groin together with the corresponding veins. In 1 instance no responses were obtained in the nerves of either the anemic or the control limb, in another there was no change in the action potentials, the femoral nerve in the anemic limb responding to stretch for three and a half hours, after which it gradually failed, while in the 2 remaining experiments increases in nervous activity were seen. In 1 case the nerve in the anemic leg and in the other that in the control leg showed the greater increase. Continued electrical activity in response to stretch for three and a half and six and a third hours respectively in the nerve to the anemic limb in 2 experiments would indicate that the leg was probably not anesthetic.

COMMENT

That the impulses described by O'Shaughnessy and Slome or those seen in the experiments reported here can be stated to be nociceptive seems extremely doubtful. Fulton⁴ described as nociceptive those impulses arising from the free nerve endings which mediate pain in response to a noxious agent. From our knowledge of fiber size and the relative size of the action potentials associated with pain compared with those of touch or proprioception, as pointed out by Erlanger and Gasser,⁵ it is unlikely that pain impulses could have been recorded for the intact animal by the methods of O'Shaughnessy and Slome or by our own methods. We have attempted to record impulses arising in response to pain by the application of a hot rod to the cat's leg. This produces only a short burst of impulses in the nerve, corresponding to touch, followed by a return to the previous level, without any recognizable impulses as evidence of the pain following such a burn. A recent investigation by Zotterman⁶ has demonstrated in thin preparations from the saphenous nerve the electrical response in the nerve following pin-prick or burning demonstrating the low amplitude of the electrical response as compared with action currents resulting from touch. If

4 Fulton I F. *Physiology of the Nervous System*. London, Oxford University Press, 1938.

5 Erlanger, I and Gasser H S. *Electrical Signs of Nervous Activity*, Philadelphia University of Pennsylvania Press 1937.

6 Zotterman N. Touch Pain and Tickling. An Electrophysiological Investigation in Cutaneous Nerves. *J Physiol* 95 1 1939.

pain impulses were recorded, one would immediately record a barrage of impulses in the nerve to the traumatized limb in experimental traumatic shock which would continue throughout the experiment instead of appearing only after three quarters of an hour to an hour after the trauma, as O'Shaughnessy and Slome have found. The possibility remains that other types of impulses, i. e., other than pain, are nociceptive. Electrical responses related to impulses in the sympathetic nervous system are even smaller than those related to pain. There is no good evidence that impulses arising in the proprioceptive or the tactile nerve endings are nociceptive.

Our experiments fail to confirm the regular presence of a barrage of impulses in the nerves of the traumatized limb, either in the saphenous or in the muscular branch. Equal increases in nervous activity have been recorded for both the traumatized and the control legs, as well as increases in the activity of the nerves to the traumatized leg and occasionally a greater increase in that of the nerves of the control leg. This may indicate that the increased impulses accompany shock rather than that they are its cause. Further suggestive evidence for this view is seen in the increased nervous activity occurring in 2 of the experiments in which shock was produced by hemorrhage alone and in anemic limb preparations for which increased nerve action potentials were recorded. These observations are in accord with those of Thompson and Kimball⁷ and of Matthews,⁸ who noted that interference with blood supply to nerve endings lowers their threshold and initiates an increased spontaneous discharge of nervous impulses. Shock produced by trauma to a limb or hemorrhage, and the preparation of an anemic limb are associated with tissue anoxia, either by peripheral vasoconstriction or by direct interference with the blood supply, and under these conditions spontaneous nerve impulses, as well as increased response to touch or stretch, may occur.

The effect of drying of the nerve, as has been pointed out by Zotterman,⁶ is to increase the signal noise ratio. This makes it difficult or impossible to compare successive records, even though the nerve is kept moistened. Varying levels of anesthesia and alteration in muscle tone in the anesthetized intact animal serve further to confuse the interpretation of recorded nervous impulses. Increases that have been observed are afferent impulses, as can be demonstrated by section of the nerves.

7 Thompson, I. M., and Kimball, H. S. Effect of Local Ischemia on Human Nerve Fibers in Vivo, *Proc Soc Exper Biol & Med* 34 601, 1921.

8 Matthews, B. H. C. Nerve Endings in Mammalian Muscle, *J Physiol* 75 1, 1933.

It is suggested that when increased nerve action potentials are recorded in the nerves to the limb in experimental traumatic shock, they may be associated with an altered metabolic state of the nerve endings resulting from the vascular changes occurring in shock and that such impulses probably arise in tactile or proprioceptive nerve endings, not in the free nerve endings for pain, and are therefore not nociceptive

SUMMARY

In shock produced by trauma to the limb of an anesthetized animal, no consistent barrage of nerve impulses has been observed in the nerves of the traumatized limb

Increased nerve impulses have been recorded in nerves of untraumatized as well as traumatized extremities

The possible origin of such impulses is discussed

SURGICAL EXCISION OF MATERIAL FOR BIOPSY IN THE LYMPHOMATOUS DISEASES

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For many years the primary lymphadenopathies, such as Hodgkin's disease, lymphosarcoma, Brill-Symmer's lymphadenopathy and the pseudoleukemic lymphomas, were diagnosed and differentiated by means of clinical signs and symptoms correlated with the history and the laboratory findings. Diagnostic tests have been devised, but none has received widespread use or acclaim, owing to variabilities and inconsistencies in interpretations and in technic. In the Memorial Hospital, histologic examination of material obtained by surgical excision is regarded as the most reliable guide for an accurate diagnosis in this group of diseases. This report is an attempt to clarify the confusion regarding certain aspects of excision, aspiration, punch and removal of a wedge as applied to biopsy in cases of the lymphomas.

In the ordinary routine of medical practice, the opportunities for excising a diseased lymph node are relatively rare. Patients who have diffuse lymphadenopathies are generally afflicted with Hodgkin's disease, lymphosarcoma, one of the leukemias or tuberculosis, more rarely, with metastatic carcinoma, sarcoma or syphilis. At the Memorial Hospital the lymphomatous diseases are concentrated in one clinic, and there is an opportunity to examine a great variety of clinical material. In addition to the new patients that present themselves for diagnosis, there is a larger group of referred patients whose cases illustrate the confusion regarding methods of obtaining material for histologic examination.

In former years the lymphomatous diseases have been the special problem of the internist. Today the proper management of the patient requires the cooperation of the internist, the surgeon, the pathologist and the roentgenologist. Present day therapy is based on (1) the histologic diagnosis, (2) the extent of the disease, (3) the response to radiation therapy, (4) the age of the patient and (5) the known clinical course of the disease in question.

Owing to the protean character of the early lymphomas, a diagnosis is often difficult to establish even with adequate material for biopsy.

From the Memorial Hospital for the Treatment of Cancer and Allied Diseases,
the Lymphoma Clinic of Dr. Lloyd F. Craver.

Clinically the patient may present only a moderate degree of local or generalized lymphadenopathy. Diagnostic tests, such as that of Gordon¹ have been advocated for the purpose of obtaining a specific reaction for the early stages of Hodgkin's disease. In general, such tests for specific reactions are still in the experimental stages and have failed to replace histologic examination of the excised lymph node. Additional confirmation may prove the value of biologic tests in cases in which examination of material obtained by surgical excision is inconclusive.

There are advocates of "punch biopsy" or "aspiration biopsy" as methods for diagnosing diseases of the lymph nodes. Experience at the Memorial Hospital has shown that examination of material obtained by aspiration from a suspected primary or secondary lymphoma is not an entirely reliable diagnostic procedure. Study of aspirated material as described by Martin and Ellis² has proved to be a valuable aid in the diagnosis of primary and metastatic cancer. The advantages and disadvantages of this method have been described by Martin and Stewart.³ The pathologist can recognize carcinoma and sarcoma from a smear of material aspirated from a lymph node, however, in the case of the lymphomas the smear may only offer highly suggestive characteristics. A differential diagnosis made from smeared material obtained from a lymphoma is difficult and often unreliable. The same difficulty applies to biopsy material obtained by punch in this particular group of diseases.

Stewart,⁴ who has had wide experience in the interpretation of biopsy material obtained by needle aspiration, advocates the method only in cases of doubtful enlargement of the lymph nodes, in order to rule out the presence of metastatic tumor. He stated that when the primary lymphadenopathies, i. e., Hodgkin's disease, lymphosarcoma, pseudo-leukemic lymphoma, Brill-Symmer's lymphoma and the like, are suspected from clinical examination and when metastatic tumor has been ruled out, it is preferable to obtain material for biopsy by surgical methods, as fixed smears, in his opinion, are unreliable in the diagnosis of the lymphomas.

Forkner⁵ reported a method of puncturing primary lesions of the lymph nodes in which he identified the material obtained by means of

1 Gordon, M. H., in Horder, T., and others. *Rose Research on Lymphadenoma*, Bristol, John Wright & Sons, Ltd., 1932, pp. 14-48.

2 Martin, H. E., and Ellis, E. G. *Aspiration Biopsy*, Surg., Gynec. & Obst. 59: 578, 1934.

3 Martin, H. E., and Stewart, F. W. *The Advantages and Limitations of Aspiration Biopsy*, Am. J. Roentgenol. 35: 245, 1936.

4 Stewart, F. W. *The Diagnosis of Tumors by Aspiration*, Am. J. Path. (supp.) 9: 801, 1933.

5 Forkner, C. E. *Material from Lymph Nodes of Man. I. Method to Obtain Material by Puncture of Lymph Nodes for Study with Supravital and Fixed Stains*, Arch. Int. Med. 40: 532 (Oct.) 1927. *II. Studies on Living and Fixed Cells Withdrawn from Lymph Nodes of Man*, ibid. 40: 647 (Nov.) 1927.

supravitally stained preparations Pavlowsky⁶ of Buenos Aires, Argentina, has written a monograph on the diagnosis of diseases of the lymph nodes. He examined material obtained by puncturing the lymph node with a needle.

In 1923, surgical excision of an involved lymph node was introduced in the lymphoma clinic of the Memorial Hospital, and it has become a routine procedure in cases in which the diagnosis is unconfirmed. In the group of atypical cases in which the results of the initial biopsy is inconclusive, repeated biopsies at a later stage of the disease generally establish the diagnosis. Many of the patients admitted for therapy have had biopsies performed elsewhere before applying to the clinic. Referred patients are required to obtain a slide of the original biopsy section for a review before treatment is outlined.

REPORT OF CASES

CASE 1—This case illustrates the difficulty occasionally encountered in diagnosing the atypical lymphomas. During three and one-half years three biopsies of material obtained by excision and 1 of material obtained by aspiration were performed before a definite histologic diagnosis was finally established (surgically excised material).

A white man aged 45 was first examined in another hospital because of a tumor in the right groin. At that time he stated that a similar mass had appeared twelve years previously. This mass disappeared after four or five months and remained absent until three years prior to his admission to this hospital. He stated that the mass had slowly enlarged during the three years of its recurrence. He was admitted to the Lincoln Hospital to the service of Dr. Bradley L. Coley, and on Jan. 6, 1934, a mass measuring 7 by 4 by 3.5 cm. was excised from the right groin. A slide of the tissue was submitted to Dr. Fred W. Stewart of the Memorial Hospital, who reported a diagnosis of inflammatory lymphoma.

On January 26 the slides were reviewed again, by Dr. James Ewing and Dr. Stewart, who reported, "Not a lymphosarcoma. This might be Hodgkin's but is not diagnosable as such. Syphilis must be ruled out and also granuloma inguinale. We cannot make a diagnosis."

Tissue was aspirated from a node in the region of the parotid gland on Nov. 2, 1936. Dr. Stewart reported, "Some type of lymphogranulomatosis with salivary gland infiltration." On November 18 a node measuring 4 by 3 by 1.5 cm. was excised from the opposite (left) groin. Histologic study showed "atrophied lymphoid tissue with fibrosis and some phagocytosed pigment."

On March 5, 1937, a node measuring 4 by 3 by 2 cm. was excised from the left femoral triangle. Dr. Stewart reported, "Giant follicular lymphoma, presumably Brill's type, but atypical and malignant looking."

Thus, after three years and three months a definite histologic diagnosis was obtained. The early failures were due not to lack of adequate material or to faulty interpretation but rather to the nature of the disease.

CASE 2—This case illustrates again the confusion in diagnosis because of features that may be regarded as interrelated in the lymphomatous disease.

⁶ Pavlowsky, A. La puncion ganglionar. Su contribucion al diagnostico clinico quirurgico de las afecciones ganglionares, Buenos Aires. *Arch. Cir. Argent.*

A white man aged 68 was admitted to the Memorial Hospital with a clinical diagnosis of either Hodgkin's disease or lymphosarcoma of the right side of the neck. There was marked involvement of the right side of the neck, with moderate generalized lymphadenopathy involving the axillas and the groins. There was no palpable enlargement of the liver or the spleen. Roentgenograms of the chest disclosed a mediastinal mass. The history of lymphadenopathy was of one year's duration. There was no history of significant pruritus or fever. Previous studies of the blood had shown values consistent with a diagnosis of lymphatic leukemia. Studies of the blood on admission showed hemoglobin, 85 per cent, red blood cells, 4,224,000 per cubic millimeter, white blood cells, 13,900 per cubic millimeter, with 39 polymorphonuclears, 57 small lymphocytes, 2 transitional cells and 2 eosinophils. A cervical lymph node was surgically excised (Feb 18, 1936), and Dr Ewing reported, "Diffuse lymphoma. Structure suggests leukemic hyperplasia." This seemed to confirm the impression of chronic lymphatic leukemia previously suggested by the blood count, despite the clinical impression of Hodgkin's disease or possibly lymphosarcoma.

The patient was treated by means of the 4 Gm radium element pack applied to the right side of the neck. There was marked regression of the disease. However, the patient refused to complete the therapy outlined and died in another institution on Sept 17, 1937. Autopsy disclosed chronic myocarditis, terminal bronchopneumonia and pulmonary edema. Microscopic sections of the lymph nodes obtained at autopsy were referred to the Memorial Hospital and were reviewed by Drs Ewing and Stewart. Histologic study showed classic Hodgkin's granuloma. A review of the previous (antemortem) biopsy, by Dr Stewart, was reported as follows: "I would surely have called it a leukemic node."

In this case, the autopsy finally confirmed the original clinical impression of Hodgkin's disease.

Wallhauser,⁷ Warthin,⁸ Craver⁹ and others have mentioned the close interrelation of the lymphomatous diseases. Craver reported a number of cases that illustrate the uncertainty of diagnosis by biopsy in these conditions and suggested an interrelation between leukemia, Hodgkin's disease and lymphosarcoma. He reported a case in which the condition had run a leukopenic course for three years and in which biopsy had shown giant follicular lymphoma. Autopsy revealed lymphatic leukemia with infiltration of the liver, spleen, stomach, kidneys, adrenals and all the superficial and deep nodes. Ultimately, after microscopic studies, the condition in this case was diagnosed as leukosarcoma. Another case reported by Craver was one of lymphosarcoma in which the diagnosis was proved by biopsy, and in which generalized symptoms developed. Autopsy revealed generalized leukemic changes.

In the atypical lymphomas the diagnosis should not be established on questionable histologic features but should be substantiated by

⁷ Wallhauser A. Hodgkin's Disease. Arch Path 16 522 (Oct.), 672 (Nov.) 1923.

⁸ Warthin A. S. Neoplastic Relationships of Hodgkin's Disease, Ann Surg 93 153 1931.

⁹ Craver L. F. Clinical Manifestations and Treatment of Leukemia. Am J Cancer 26 124 1936.

definite confirmatory proof. Biopsy material obtained at intervals during the course of the disease is especially desirable in the presence of conditions which tend to run a pseudoleukemic course.

SELECTION OF BIOPSY MATERIAL

It is important in a given case to select a typically diseased lymph node for excision. One must attempt to distinguish diseased or involved nodes from simple regional lymphadenopathies associated with infected teeth or diseased tonsils and from nodes that may be considered within normal limits.

It is undesirable to excise an irradiated lymph node for the purpose of establishing a histologic diagnosis. If a biopsy has not been performed, an attempt should be made to find a suitable untreated node which shows evidence of being involved in the disease process. If no such node is available, the biopsy should be deferred until new or suitable nodes appear. Treatment should be started, however, on the basis of available clinical data. In patients who have been irradiated the node selected for excision should be situated outside the field of the previous radiation therapy.

Occasionally, small, discrete involved nodes will be found adjacent to the site of a bulky conglomerate mass. These nodes are generally freely movable and easily excised; they are the nodes of choice. A node smaller than 1 cm in diameter may not prove typical of the disease. Small, friable nodes are easily traumatized and destroyed in removal. The node of choice measures approximately 1.5 to 2 cm in diameter, is freely movable and is not adjacent to important nerves or vessels.

SITE OF ELECTION

The neck is the site of election for surgical excision of material for biopsy in the widely disseminated lymphadenopathies. The advantages of the cervical region are (1) ease of excision, (2) freedom from irritation and wound infection and (3) ease of postoperative dressing and care.

The most superficial of the lymph nodes that appear involved should be selected for removal. Nodes situated along the lateral border of the trapezius muscle should be avoided. Capable surgeons have injured the spinal accessory nerve during the dissection of a lymph node located along the border of this muscle. It is important to remember that the axillary and inguinal nodes are more intimately associated with the larger lymphatic vessels and that dissections in the axilla and in the groin increase the hazards of postoperative drainage of lymph. These areas should be avoided if possible. Hair follicles and sweat glands predispose to infection. In the event that the disease is limited to the axillas or to the groins, special care should be used in aseptic technique.

ATTITUDE OF THE SURGEON

Surgical excision of a diseased lymph node is regarded by some surgeons as an operation of minor importance. Such a procedure is generally delegated to a junior intern, often without advice. It is not my purpose to dramatize excision of material for biopsy as a technical procedure. However, the casual order, "excise node for biopsy specimen," should be condemned. The attending surgeon should stress (1) the importance of carefully selecting typical material for the benefit of the pathologist and (2) the importance of approaching the problem from the point of view of the histologic, clinical and cosmetic results.

Often such minor operations are performed hurriedly. Incisions are made much larger than necessary, frequently in violation of all rules



Fig 1—A, injudicious incision for removal of tissue for biopsy. B, injudicious exploratory incision.

of plastic and cosmetic surgery (fig 1). Undesirable postoperative complications such as hematoma, infection and lymph drainage are the telltale signs of injudicious surgical procedures.

Craver¹⁰ recalled 1 patient in whom the physician accidentally severed the spinal accessory nerve during the removal of a cervical lymph node. Ewing, in a personal communication, cited an almost fatal hemorrhage which followed the removal of a lymph node. The surgeon had performed a hurried operation and had allowed the patient to return home, where she became exsanguinated. I have seen 2 patients in whom persistent drainage of lymph followed the use of plain catgut ligatures in the region of the groins. In both of these patients profuse drainage of lymph persisted for a week to ten days despite pressure

¹⁰ Craver, L. F. Personal communication to the author.

and attempts to control the drainage without opening the wound. In the admitting department of the Memorial Hospital it is a rather common experience to see patients referred for diagnosis and treatment who exhibit large tumors that are infected and fungating because of injudicious exploratory incisions (fig 2). In general, these patients have had one or more incisions made by a family physician under the false impression that the swelling was due to localized inflammation. All enlargements of lymph nodes and lymph node-bearing areas should receive cautious consideration, and in no instance should a tumor or a swelling be indiscriminately incised. Frequently wounds have been

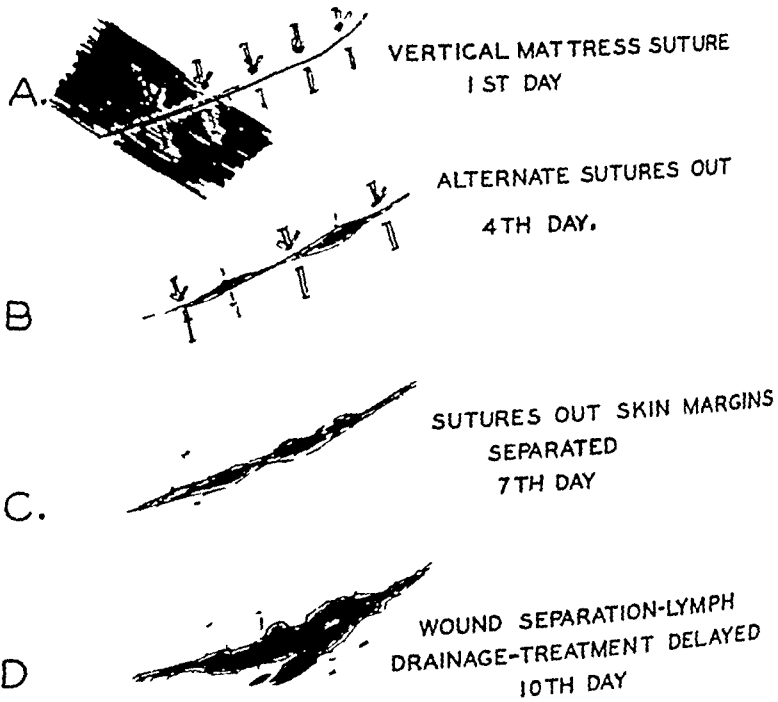


Fig 2—Incorrect technic

erroneously packed wide open or drained. In such instances the diagnosis of neoplasm becomes obvious when the growth fungates through the open wound. Infection and fungation add to the miseries of both the patient and the surgeon. Excision of tissue for biopsy belongs to the field of cancer surgery, and in this type of procedure caution and thoroughness are of more importance than haste.

TECHNICAL SUGGESTIONS

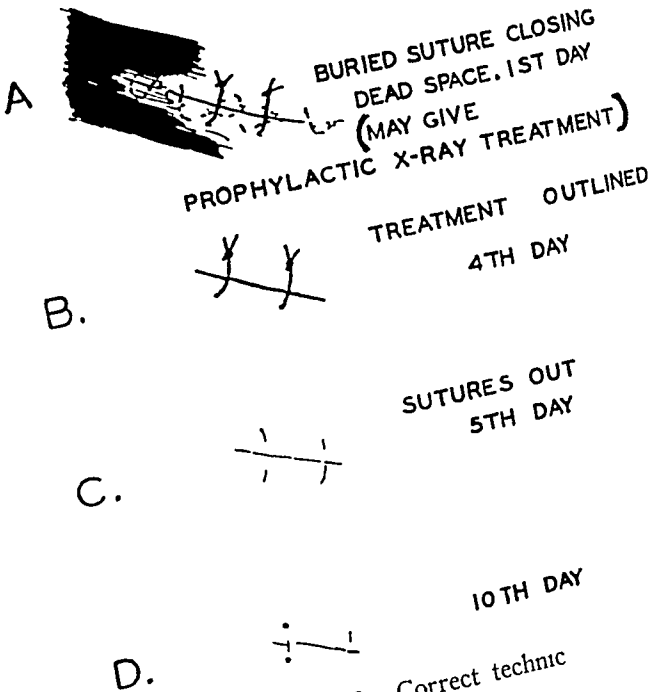
To remove a lymph node intact through a small incision requires time and a certain degree of patience and dexterity. There are, of course, theoretic objections to a cramped technic. For example, 1 Unnecessary trauma may result from an operation performed through an inadequate surgical exposure. 2 Large incisions are avoided to

quickly as small ones. 3 A cramped technic is unnecessary and makes a time-consuming operation of a simple procedure. Certain of these criticisms are well taken, however, the general standard of results seems to justify a more cautious attitude regarding excision of material for biopsy, with particular reference to the lymphomatous diseases.

No attempt should be made to excise a deeply situated node through a tiny incision. Particularly is this true in dealing with axillary or femoral nodes in an obese patient. If a node in the axilla or the groin is the only available source of biopsy material, one should have adequate surgical exposure. The larger dilated lymphatics should be doubly ligated with nonabsorbable suture material, they occasionally require the additional precaution of a suture ligature. Ordinary plain catgut ligatures may become soft and cause distressing lymph drainage. A poorly ligated lymph vessel will drain for days unless steps are taken to control it. The condition is annoying to the patient and requires frequent changes in the dressing. The moisture makes the application of a tight compression bandage (groin or axilla) a difficult problem. In large incisions this complication predisposes to infection, wound separation and fungation. Once a wound starts draining lymph, a carefully placed secondary combined skin and subcutaneous suture of the vertical mattress or so-called on end mattress type generally controls the drainage and holds the edges of the wound intact. More or less lymphedema results. Careful silk technic in ligating the major lymph vessels prevents postoperative lymph drainage. The theoretic objection to the use of nonabsorbable ligatures as regards infection and sinus formation presupposes a rigid aseptic surgical technic.

Points of technical value are: 1 A few cubic centimeters of 0.5 per cent or 1 per cent solution of procaine hydrochloride should be injected along the deeper structures before the blood and lymph vessels associated with the node are clamped. The ordinary infiltration sufficient to anesthetize the skin may not render the deeper vessels and nerves insensitive to the trauma of division and ligation. 2 The skin sutures should be left in situ longer than usual if radiation therapy is started within a day after operation. Early removal of skin sutures plus early irradiation favors separation of the cutaneous margins, poor healing and the possibility of infection and tumor fungation (fig. 2). There are no objections to the early application of roentgen rays if the cutaneous incision is small and if the sutures are left in situ until healing is firm (fig. 3).

Occasionally lymphomas appear as solitary tumors in the cervical, axillary, inguinal or femoral regions and may be fixed and not suitable for total removal (fig. 4). Careful examination may not reveal a suitable node for excision. In such masses a punch may enable one to



In the presence of such a growth material may be obtained by aspiration or by removal of a wedge of tissue

obtain sufficient material for a routine paraffin section. As has been mentioned, the smear method of examining tissue is not advisable in cases of lymphoma, but if sufficient material is obtained a quick smear may show highly suggestive histologic features of the disease. In such selected cases radiation therapy may be instituted as a therapeutic test. However, an attempt to obtain tissue for a routine section should be made at some future date. If physical examination does not reveal a suitable node for excision and if the tissue obtained by punch definitely fails to establish the histologic diagnosis, one must resort to the undesirable "wedge biopsy." It is very important, especially in the presence of a solitary mass in the neck, to visualize carefully the oral cavity, the nasopharynx, the hypopharynx and the larynx for evidence of a primary tumor.

In excision of a wedge also a small cutaneous incision is desirable. The incision should be made at the margin of the tumor rather than directly over the mass. The exposure should be adequate to insure safe removal of a typical wedge of tumor tissue. Palpation through the wound is not a reliable guide to tumor tissue. The glistening surface of the tumor should be visualized and the tumor mass identified by direct vision. Attempts at blind removal of a wedge of suitable material by feel should be avoided. A wedge of tissue may be obtained and a defect palpated in the remaining mass, but prepared sections frequently reveal that the specimen consists only of surrounding fat and fibrous capsule.

Large, slowly growing tumors are often surrounded by a rather resistant layer of connective tissue and fat. This layer of adipose tissue together with the deeper fibrous tissues should be carefully incised and retracted in order to expose the true capsule of the tumor. Lymphomas are generally friable and soft, therefore it may facilitate matters to sacrifice a portion of the true capsule in the wedge. The actual incision into the tumor should be as far removed from the cutaneous incision as is feasible and consistent with the exposure. A sharp scalpel should be used to excise the wedge, the specimen should be removed without trauma. The cautery, the electric knife or rough handling tends to destroy and distort the histologic character of the biopsy specimen. Postoperative fungation of the wound is minimized by shutting the fibrous capsule and obliterating the defect with adipose tissue. The skin should be approximated with fine silk or dermal sutures and the wound closed without drainage.

COMMENT

Two groups of patients are compared (tables 1 and 2) in which different techniques for excising lymph nodes for biopsy were employed, group 1 in which silk and a more or less cramped technic were used and

group 2, in which catgut and a less confining technic were employed. The results in group 1 showed excellent wound healing with cosmetically good scars and an average interval between biopsy and the onset of

TABLE 1 (Group 1)—Small Incisions and Silk Technic

Patient	Sex	Surgical Excision of Tissue	Institution of Radiation Therapy	Interval Between Biopsy and Institution of Therapy, Days	Histologic Diagnosis
B H	M	1/13/37	1/18/37	5	Hodgkin's disease
A T	F	1/28/37	1/28/37	0*	Reticulum cell lymphosarcoma
M C	M	2/18/37	2/25/37	7	Hodgkin's disease
J G	M	3/ 8/37	3/12/37	4	Reticulum cell lymphosarcoma
A R	M	3/ 9/37	3/12/37	3†	Giant follicle cell lymphosarcoma
I S	M	4/ 2/37	4/ 6/37	4	Hodgkin's disease
B K	M	4/30/37	5/ 5/37	5	Hodgkin's disease
A G	F	5/18/37	6/14/37	6	Reticulum cell lymphosarcoma
S S	M	6/ 9/37	6/22/37	5	Hodgkin's disease
A M	M	6/15/37	6/29/37	7	Lymphosarcoma
E M	F	6/25/37	7/19/37	7*	Hodgkin's disease
J L	F	7/12/37		7*	Reticulum cell lymphosarcoma

(Average, 4 7)

* Wedge biopsy (previous doubtful aspiration biopsy)
† Suggestive aspirations

TABLE 2 (Group 2)—Large Incisions and Catgut Technic

Patient	Sex	Surgical Excision of Tissue	Institution of Radiation Therapy	Interval Between Biopsy and Institution of Therapy, Days	Histologic Diagnosis
R W	M	1/29/36	2/ 4/36	6	Lymphosarcoma
F V	M	2/10/36	2/16/36	6	Hodgkin's disease
W S	M	2/18/36	2/24/36	6	Lymphatic leukemia
V G	M	3/27/36	4/ 1/36	5	Hodgkin's disease
M B	F	4/20/36	4/27/36	7	Hodgkin's disease
F P	F	6/ 8/36	6/19/36	11*	Lymphosarcoma
A H	M	8/ 5/36	8/ 5/36	0†	Hodgkin's disease
E C	M	8/28/36	9/ 3/36	6	Hodgkin's disease
C L	M	10/28/36	11/ 3/36	6	Hodgkin's disease
A S	M	11/27/36	12/ 8/36	11*	Hodgkin's disease
L G	F	2/ 5/37	2/19/37	14*	Hodgkin's disease
Sy S	M	2/11/37	2/20/37	9	Giant reticulum cell lymphosarcoma
D F	M	3/29/37	4/ 6/37	8	Hodgkin's disease
R L	M	5/ 7/37	5/13/37	10*	Hodgkin's disease
L J	F	5/19/37	6/23/37	7	Hodgkin's disease
N L	M	6/15/37	7/ 1/37	8	Reticulum cell lymphosarcoma
J W	M	6/18/37		13*	

(Average, 6 1)

* Cases omitted in computing average interval
† Suggestive aspirations

treatment of four and seven-tenths days. The results in group 2 were gratifying, with delayed healing, drainage of lymph and an average interval before treatment of six and one-tenth days. The 12 patients in group 1 were managed by the same surgical technic in the beginning the technic was used for cosmetic reasons.

and without any definite idea of speeding up the application of roentgen therapy. It was then observed that the patients had very little reaction around the wounds. The incisions were healed and ready for roentgen therapy approximately on the day that the histologic report became available (four day interval). The minimum wound reaction and the rapid healing in the patients of group 1 seemed to indicate that immediate roentgen therapy probably would not have altered wound healing. No more than three skin sutures were used, and in most instances only two were used. In 4 of the 12 patients the skin was approximated with a single suture. In general, the conclusions from this comparison are summarized in table 3.

Eleven different surgeons performed the 17 biopsies in group 2. Eight surgeons performed 1 biopsy each, one surgeon performed 2, one 3 and another 4. Therefore, for strictly comparative results between catgut and silk technic or for any other particular feature of surgical

TABLE 3—*Comparison of Results with Different Techniques*

	Silk Technic—Small Incisions		Catgut Technic—Large Incision	
	Advantages	Disadvantages	Advantages	Disadvantages
Patient	Negligible scar Minimum complications Minimum delay	None	None	Ugly scar Wound may fester Infection
Surgeon	Favorable results	Time consuming	Technically easy	Longer postoperative care more complications

technic these results are of little value and are presented only for their general interest as related to the problem of biopsy in the lymphomatous diseases. As may be noted in table 2, 5 of the cases are omitted in computing averages because of the unusually long delay before treatment was started. Ordinarily the interval between biopsy and the institution of therapy is approximately four days (interval for routine section). The decision to begin or to delay therapy may be due to the condition of the wound or to the patient's inability to fill an early appointment, due to employment, distance from the hospital, sickness in the family, bad weather or holidays. Also, the general physical condition may be such that a delay in treatment is deemed advisable in order to allow the patient to recover from a temporary secondary infection.

Such factors as those mentioned should apply about equally to both group 1 and group 2 despite the small sampling of patients. In group 2 5 of the 17 patients had a delay of ten days or more owing to a combination of poor healing, weakness, lymph drainage and the other general causes of delay mentioned. Discounting these 5 patients the residual 12 in group 2 when compared with the 12 of group 1 showed an average delay of an additional day and a third.

In 1 instance in each of the two groups treatment was started the day surgical excision of biopsy material was performed, owing to suggestive histologic evidence obtained from previous needle aspirations. The aspirations had been performed during an earlier stage of the disease, in which lymph nodes were inaccessible for excision. Subsequently, in 1 instance a "wedge biopsy" was performed, in the other a deeply situated node was dissected free and excised.

SUMMARY AND CONCLUSIONS

At the Memorial Hospital, surgical excision of an involved lymph node is the method of choice for obtaining biopsy material in the lymphomatous diseases. For certain patients it is necessary to repeat the procedure during the course of the disease in order to establish a definite diagnosis.

In this group of diseases, needle puncture and aspiration are reserved for patients in whom there are no accessible diseased lymph nodes suitable for excision and for whom removal of a wedge is not feasible. Smears of aspirated material are supplemented when possible by additional biopsy material obtained during the course of the disease.

The selection of a suitable diseased lymph node for surgical removal deserves the careful attention of the clinician.

Adequate small cutaneous incisions and careful aseptic silk technic minimize the undesirable postoperative complications of lymph drainage and wound separation.

MUSCULAR AND SKELETAL CHANGES IN ARACHNODACTYL

JOHN J FAHEY, M D

CHICAGO

The syndrome now designated as arachnodactyly was first described by Marfan¹ in 1896. His patient, a girl 5½ years of age, had increased length and slenderness of the hands and feet, decrease in soft tissue, finger contractures, ligamentous relaxation and other associated congenital abnormalities. Because of the long, thin spider-like feet he called the condition "pieds d'araignee." The term arachnodactyly ("spider digits") was first used by Achard² in 1902.

Young³ reviewed 22 cases of arachnodactyly reported between 1896 and 1929 and added 4 cases. Weve⁴ in 1932 described 23 cases in six families, bringing the total number of cases reported at that time to 84. He emphasized the familial and hereditary characteristics of the condition. Since Weve's report 48 cases have been added to the literature. Reports of only 37 cases have appeared in the American literature since Piper and Irvine-Jones⁵ described their case in 1926. Pediatricians gave most attention to this condition until Ormond⁶ in 1924, emphasized the important ophthalmologic features. Since that time the majority of reports have appeared in the ophthalmologic journals and have dealt chiefly with the ocular findings. The abnormalities associated with arachnodactyly are not ordinarily detected until the second or third year of life. There is either actual or apparent lengthening of the hands and

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1 Marfan A B. Un cas de deformation congenitale des quatre membres plus prononcee aux extremités caracterisee par l'allongement des os avec un certain degre d'amincissement, *Bull et mem Soc med d hop de Paris* **13** 220, 1896.

2 Achard C. Arachnodactylie, *Bull et mem Soc med d hop de Paris* **19** 834, 1902.

3 Young M L. Arachnodactyly, *Arch Dis Childhood* **4** 190, 1929.

4 Weve H. Ueber Arachnodactylie (Dystrophia mesodermalis congenita Typus Marfan), *Arch t Augenh* **104** 1 1931.

5 Piper R K and Irvine-Jones E. Arachnodactylia and Its Association with Congenital Heart Disease. Report of a Case and Review of the Literature, *Am J Dis Child* **31** 832 (June) 1926.

6 Ormond A W and Williams R G. Arachnodactyly with Special Reference to Ocular Symptoms, *Guv & Hosp Rep* **74** 385 1924.

feet, particularly the fingers and toes. The face may have an appearance of maturity because of a decrease of subcutaneous tissue. Roentgenograms of the hands and feet usually show long, thin bones with a decrease in soft tissue. The patients grow rapidly in height. Skeletal development is in advance of chronologic age in many cases. The soft tissue about the extremities is poorly developed. There are ligamentous relaxation and, occasionally, contractures of the fingers. Spinal curvature in early childhood is common. Dislocation of the lenses associated with other ocular anomalies has been found in over half the reported cases. The external ear may be large, with poorly developed cartilaginous structure. The palate in many cases is curved and highly arched. The intelligence in most instances is normal. The condition may be sporadic or familial. The incidence in the two sexes is equal.

REPORT OF CASES

CASE 1—G. D. (fig 1), a boy aged 5½ years, was brought for examination because of weakness, thinness of the extremities, curvature of the spine and nearsightedness. He was delivered at full term by instruments but without difficulty. The weight at birth was 7 pounds and 10 ounces (3,405 Gm.). The child started to walk at 13 months of age, and the gait was always unsteady. The parents believed that he was not as strong as other boys of the same age and observed that he was near-sighted. Curvature of the spine was first noticed during the fourth year and had gradually progressed. The patient was an only child. The parents, who were of Greek origin, showed none of the characteristic abnormalities of arachnodactyly, and no evidence of the disorder could be found in other members of the family.

Examination—The patient was very tall for his age, the standing height was 55.4 inches (140 cm.) and the weight 59 pounds (26.8 Kg.). The gait was unsteady. The skull was symmetric except for slight prominence of the forehead. The ears were large. The teeth were normal. The palpebral fissure of each eye was oblique, this peculiarity being more marked on the right side. The external conjugate movements of the eyes were full and synchronous. The tactile reaction was normal. There was no abnormality of the cornea of either eye. The iris was tremulous in both eyes. The lenses were clear and were dislocated downward and temporally. The zonular fibers were seen in the aphakic portion of the lens. The fundi were normal. The vision was not improved by lenses. The palate was highly arched and narrow. Mild "right dorsal and left lumbar scoliosis" (fig 3A) was present. The pelvis appeared broad. The subcutaneous tissue of the extremities was decreased, exaggerating the length of the limbs (fig 2). Measurements did not reveal, however, that the bones of the hands and feet were relatively increased in length as compared to the long bones of the arms. The fingers could be extended 20 degrees beyond the normal limits at the metacarpophalangeal joints. A similar but less marked relaxation was noted in other finger joints. A roentgenogram of the spine (fig 3A) showed thoracolumbar scoliosis. Roentgenograms showed the bones of the right forearm and hand (fig 3B) and the right foot (fig 4B) to be advanced in development. The bones of the

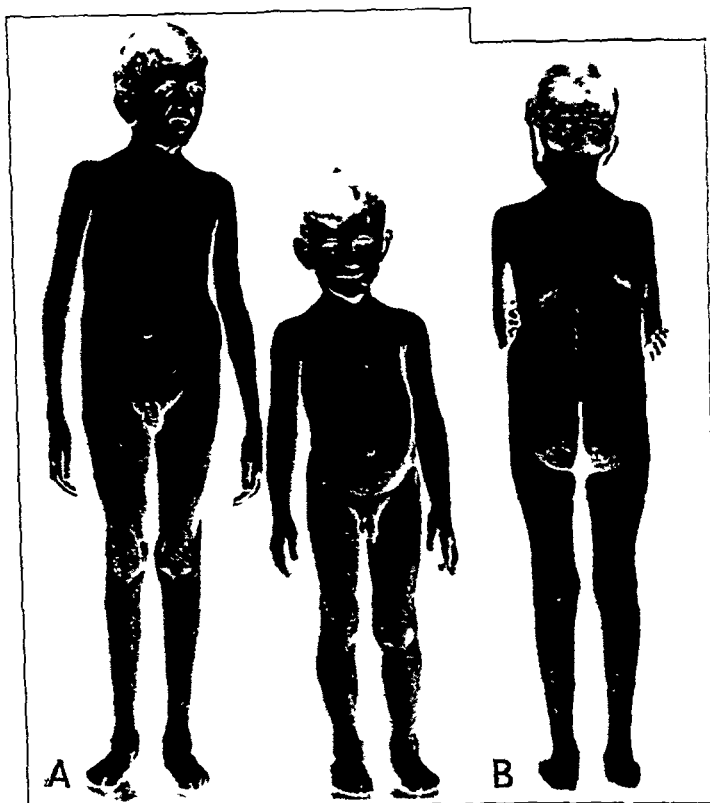


Fig 1 (case 1) — *A* comparison of G D, a boy aged 5½ years (left), with a normal child of the same age. Note the long, thin extremities, the large ears and the oblique position of the eyes. *B*, posterior view, showing dorsal scoliosis toward the right, with winging of the scapulas. The loose adipose tissue about the hips is well visualized. Bilateral dislocation of both lenses and iridodonesis are present.

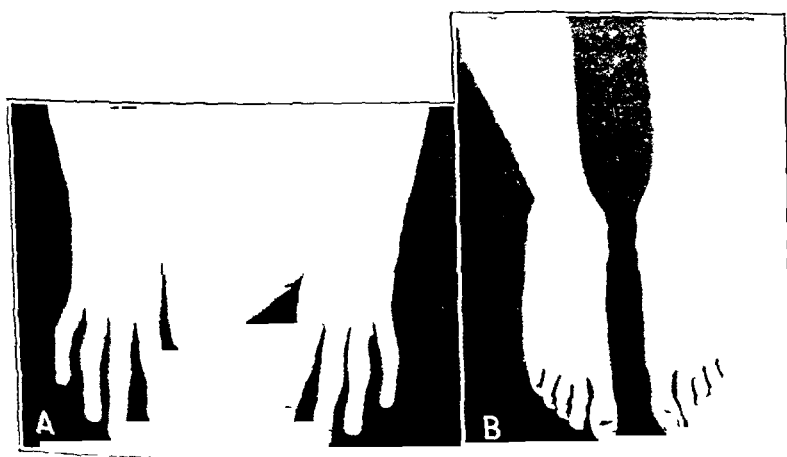


Fig 2 (case 1) — *A*, hands of the patient. The fingers are long with thin soft parts. *B*, photograph of the feet, showing pronation and long, thin toes. General ligamentous relaxation is present.



Fig 3 (case 1) —*A*, roentgenogram of the spine, showing thoracic scoliosis toward the right *B*, roentgenogram of the right forearm and hand of the patient (right) in comparison with those of the same normal child (left) as in figure 1 *A*. The bones of the upper extremities are developed out of proportion to the age. All centers of ossification in the carpus bone are present, while in the normal child only three are well ossified.

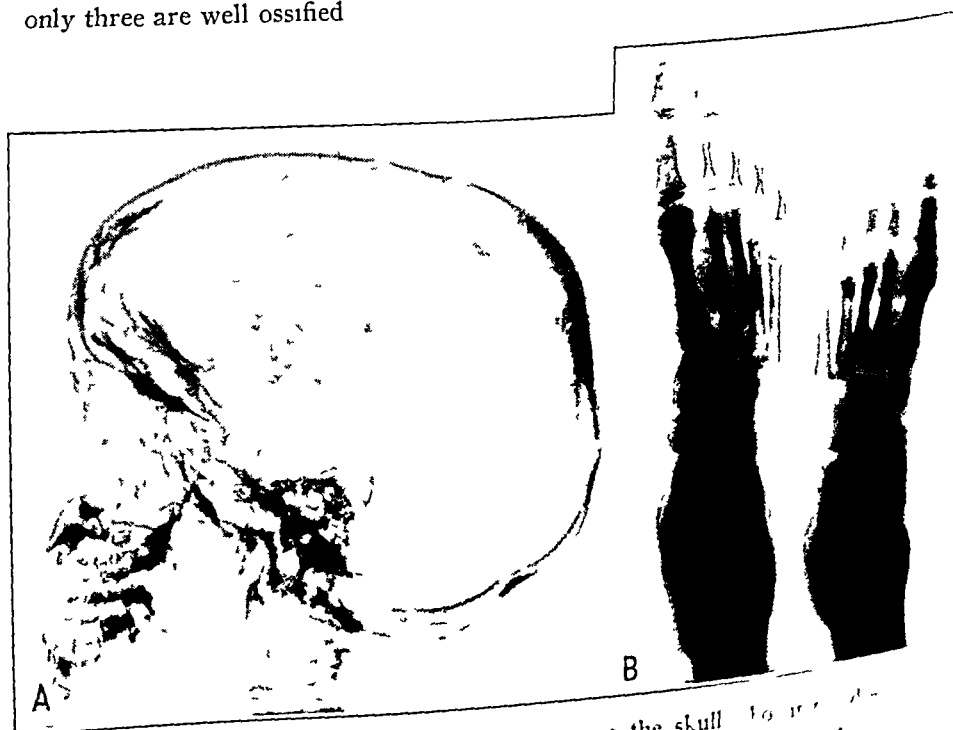


Fig 4 (case 1) —*A*, lateral roentgenogram of the skull showing the occipital protuberance and a small anterior fossa *B*, roentgen comparison of the forearm and hand bones of the patient (left) and those of the normal child. The bones of the patient are relatively thinned.

were narrowed out of proportion to their length. A roentgenogram of the skull (fig 4 A) showed a slightly deepened sella. The sinuses were large, and the anterior cranial fossa was decreased. Routine examination of the blood and urine showed them to be normal. The value for blood calcium was 11.03 mg and that for phosphorus 3.88 mg per hundred cubic centimeters. Microscopic study of tissue removed from the gastrocnemius muscle showed it to be of normal structure. The intelligence quotient was 96 (Stanford Binet).

CASE 2—M. P. (fig 5 A), a girl aged 25 months, was seen because of poor general health, deformities of the hands and feet and poor vision. She was an only child, born of parents in the fourth decade. At infancy it was noticed that the hands and feet were long and slender. She walked at 18 months. Five months

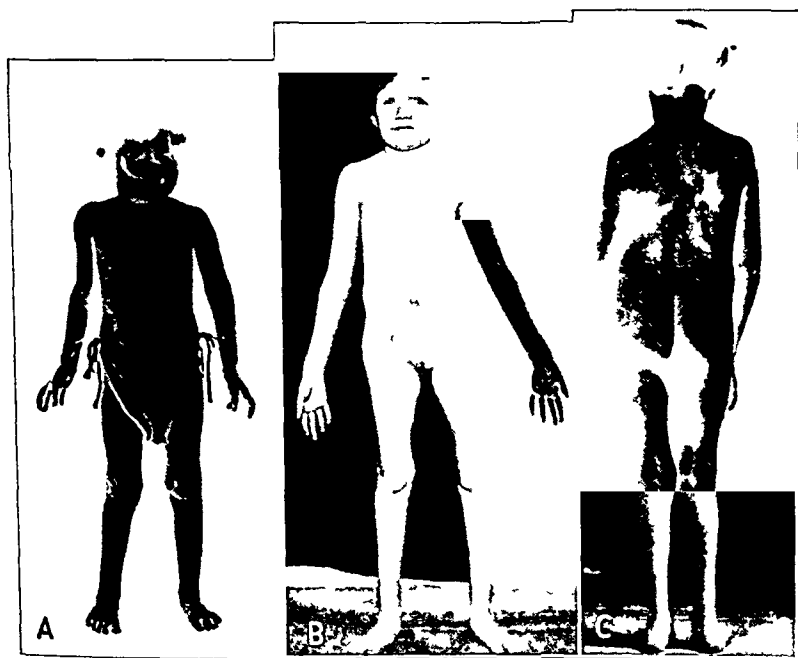


Fig 5 (case 2)—A. M. P., a girl aged 25 months. Note the long slender hands and feet and the thinness of soft tissue of the extremities, particularly the fingers and toes. Subluxation of both lenses, iridodonesis and hydrophthalmos are present. B. same patient at the age of 5 years and 2 months. The feet are pronated and there is general relaxation of the ligaments. C. posterior view, showing thoracic scoliosis on the right and lumbar scoliosis on the left.

prior to observation a spinal curvature was first observed. Visual disturbance had been present for several months. The mental development was normal. There was no family history of similar difficulty.

Examination.—The head was slightly larger than normal but was symmetric. The ocular movements were normal. The palpebral fissures were equal. Each corner measured about 14 mm in horizontal and in vertical diameter. The

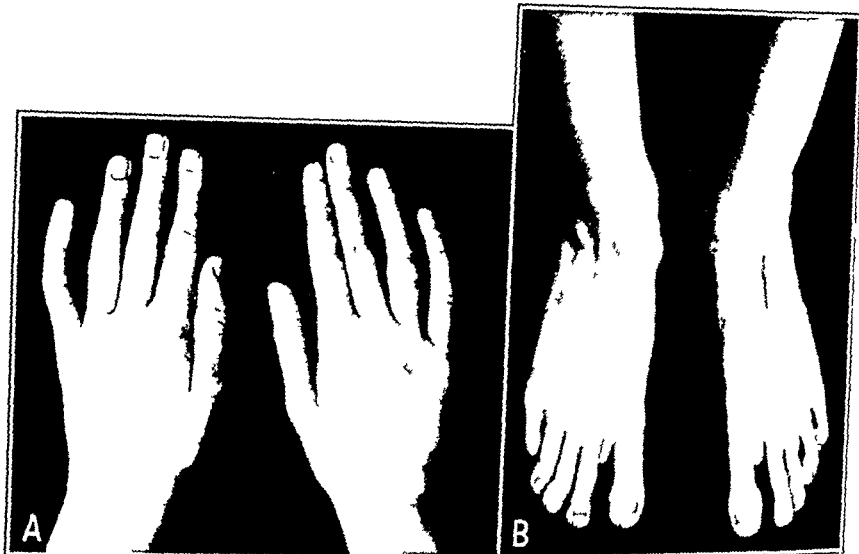


Fig 6 (case 2) —*A*, hands of M. P., showing the long slender fingers and toes. *B*, feet of the same patient. The feet are pronated, long and slender. The phalanges are exaggerated in length by the thinness of the soft tissue.

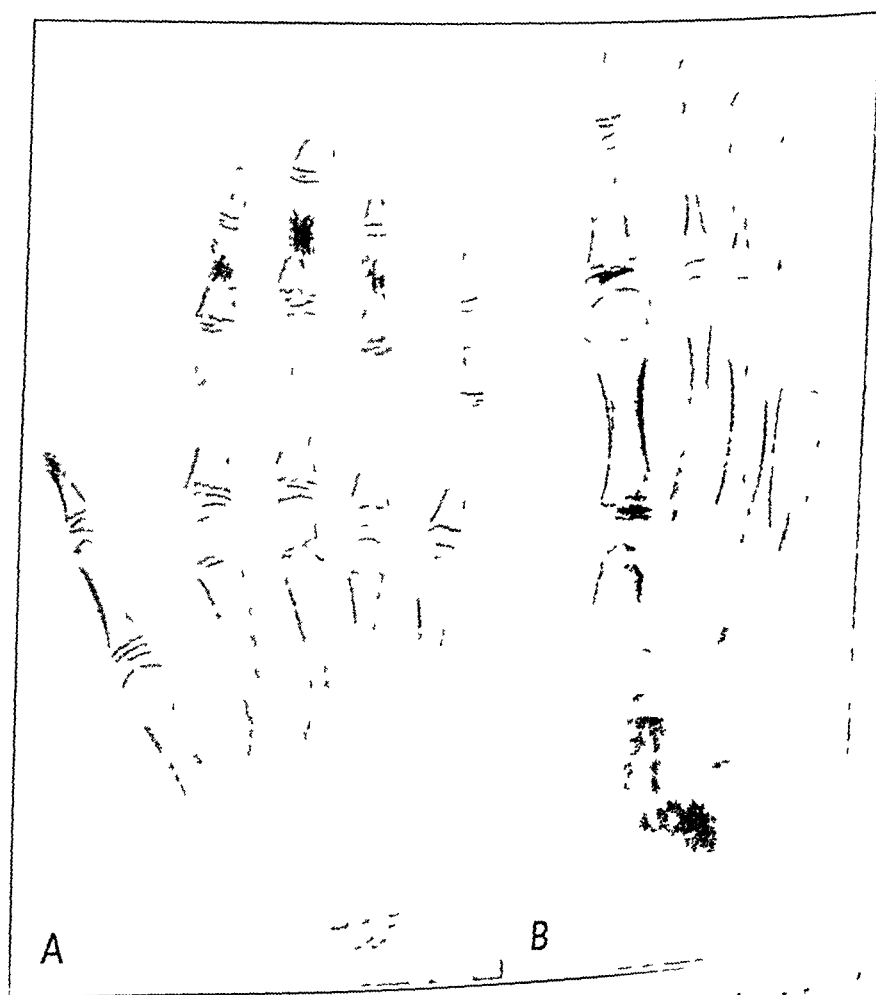


Fig 7 (case 2) —*A*, roentgenogram of the right hand, showing the metacarpals and phalanges, with a decreased soft tissue shadow. *B*, roentgenogram of the foot, showing mild thinning of the bones of the foot (*B*). The phalanges of the foot are deformed.

anterior ocular chambers were extremely shallow. The irises were tremulous and somewhat atrophic as demonstrated by transillumination. The right pupil measured 1 mm and the left 2.5 mm in diameter. The tactile tension was normal in both eyes. The right pupil dilated to 3 mm on administration of atropine, but no increase in size was noted in the left. Both lenses were dislocated upward and outward. The right disk had a temporal conus, but no temporal pallor of either disk was seen, and there was nothing to suggest glaucomatous excavation. A diagnosis of hydrophthalmos and subluxation of each lens was made. The palate was high and narrow. Dentition had proceeded normally. Mild scoliosis to the

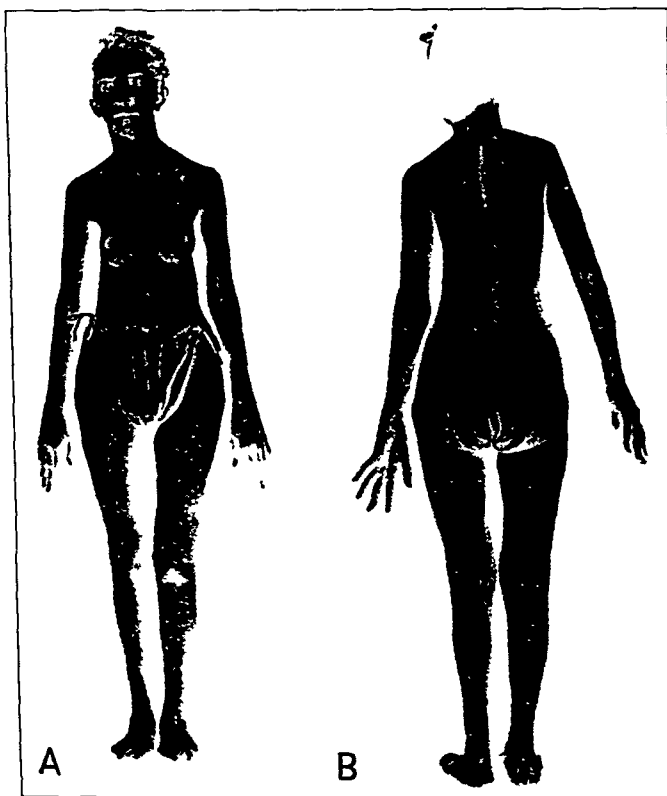


Fig 8 (case 3) — J. M. S., a girl aged 15 years, with upward and inward dislocation of both lenses, myopia and bilateral iridodonesis. Note the pigeon breast deformity and the long slender hands and feet. B: mild curve in the lower thoracic portion of the spine, with prominence of the right scapula. Hyperextension of some of the terminal phalanges is present due to ligamentous relaxation.

right in the dorsal region was present. The feet and hands appeared long and slender, particularly the fingers and toes. There was a blunt projection of soft tissue between the first and second toes of both feet and one lateral to the base of the third left toe. Because of ligamentous relaxation the range of motion was abnormally great in the joints of the hands and feet. A decrease of subcutaneous tissue exaggerated the length of the fingers and toes. Neurologic examination gave negative results.

The patient was again seen when she was 5 years of age, because of increasing scoliosis. A roentgenogram (fig 7) of the right foot at that time showed no evidence of bony deformity at the site of the soft tissue prominences. The metacarpal bones, metatarsal bones and phalanges were long and narrow, and the soft tissue about them was decreased. The narrowing was especially noticeable near the center of the diaphysis. Bowing of the fifth finger and phalangeal deformities



Fig 9 (case 3)—*A*, foot of M. S. The second and third digits are extended to show the web contracture of the skin on the ventral surface. *B*, lateral roentgenogram of the skull, showing a normal sella.

of the fifth toe were present. All the centers of ossification were well developed and were in advance of the child's age. Roentgenograms showed no abnormality of the skull.

CASE 3—M. S. (fig 8), a girl aged 15 years, came to the clinic because of frequent attacks of headache. She had worn glasses since the age of 10.

She stated that the optimum distance for reading was 4 inches (10 cm). As far back as she could remember, friends had remarked about her long feet and hands. Her father, mother, two brothers and two sisters had ocular defects but no skeletal manifestation of arachnodactyly.

Examination—The skull was of normal shape. The left eye was slightly higher than the right. The anterior chambers were deeper than normal. The lenses were dark red with a black rim. They were dislocated upward and inward and occupied four fifths of a 6 mm oval pupil. The remaining one fifth of each pupil formed a crescent of clear red through which the fundi could be seen. Dentition

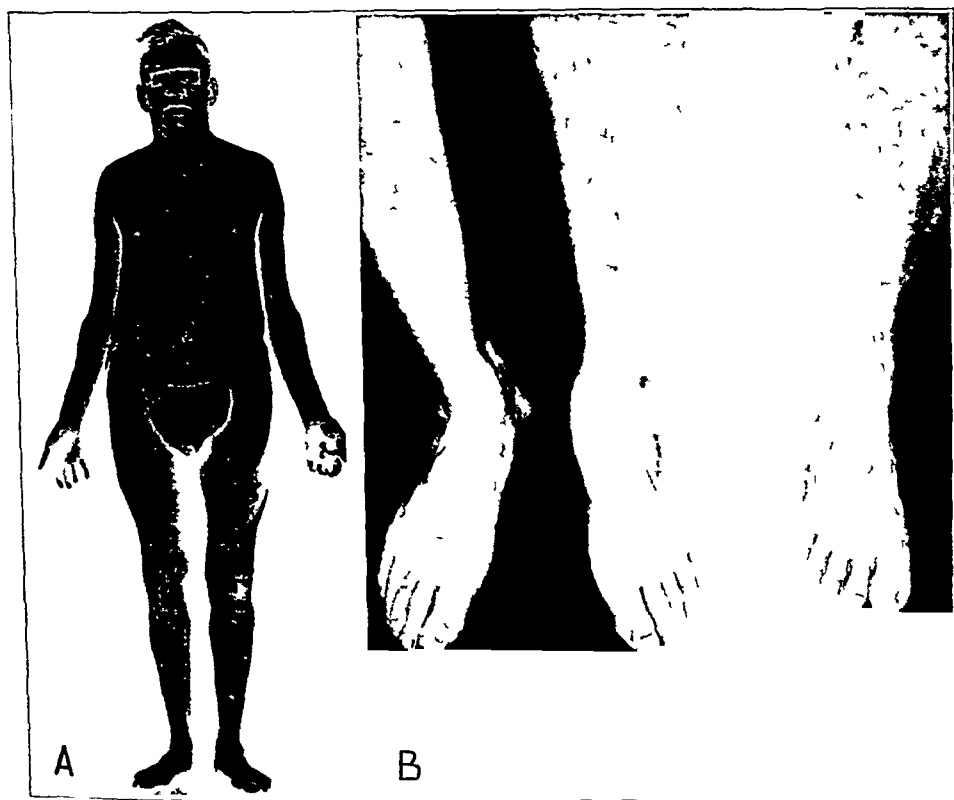


Fig 10 (case 4)—A, M T, a man aged 46 years. Blindness in the right eye resulted from uveitis peracta. Note the long slender extremities with muscle thinness which is exaggerated on the distal portion of the extremities. Note the wide pelvis. B, feet of the same patient (left) contrasted to a normal adult's foot.

was normal. The palate was high, narrow and arched, curving anteriorly to the right. A pigeon breast deformity was present (fig 8A). The heart and lungs were normal. There was a mild dorsal curvature with the usual prominent right scapular flare (fig 8B). The extremities appeared longer and were thinner than normal. The hands were long and slender but not relatively increased in length as compared to the other long bones. The thinness of the soft tissue was most marked about the fingers. Contracture of the soft tissue on the palmar surface of